

Tuberculosis Control in Alaska

Tuberculosis incidence (per 100,000 population),
Alaska and U.S.; 1991-2000



July 2001

Tuberculosis Control in Alaska



"To Eliminate Tuberculosis in Alaska"

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State of Alaska
Tony Knowles - Governor
Department of Health and Social Services
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July 2001

Important Telephone Numbers

1. Section of Epidemiology - Tuberculosis Control Program: 1-907-269-8000
fax 1-907-563-7868
2. Section of Epidemiology - 24 hour emergency number: 1-800-478-0084
3. Rapid Telephonic Reporting System for disease reporting: 1-800-478-1700 (statewide)
1-907-561-4234 (Anchorage)
4. State Public Health Laboratory, Anchorage: 1-907-334-2100

5. Public Health Centers:

Anchorage	343-4799	Ketchikan	225-4350
Barrow	852-0270	Kodiak	486-3319
Bethel	543-2110	Kotzebue	442-7144
Craig	826-3433	Nome	443-3265
Delta Junction	895-4292	Petersburg	747-4611
Dillingham	842-5981	Seward	224-5567
Fairbanks	452-1776	Sitka	747-3255
Fort Yukon	662-2889	Tok	883-4101
Galena	656-1200	Valdez	835-4612
Haines	766-3300	Wasilla	376-2437
Homer	235-8857	Wrangell	874-3615
Juneau	465-3353		
Kenai	283-4871		

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Table of Contents

Preface	6
Frequently Asked Questions	7
Strategy for the Elimination of Tuberculosis in Alaska	11
Alaska Division of Public Health strategy for the elimination of tuberculosis	11
Components of Alaska’s Tuberculosis Control Program	11
Key activities	12
Bacteriology and Pathogenesis	15
Bacteriology	15
Transmission of tubercle bacilli	15
Pathogenesis of tuberculosis	16
Infectiousness of patients with pulmonary tuberculosis	17
Extrapulmonary tuberculosis	18
Tuberculin Skin Testing	19
The Mantoux skin test	20
Standard technique for intradermal application of the Mantoux test	20
Interpreting the Mantoux skin test	21
Multiple-puncture skin tests	22
False negative skin tests	22
BCG vaccine	23
The booster phenomenon	24
Adverse reactions	25
Contraindications	25
Anergy testing	25
Treatment of Latent Tuberculosis Infection	27
Persons for whom treatment of latent tuberculosis infection is recommended	27
Fundamentals of treatment of latent tuberculosis infection	29
Treatment of HIV-negative adults	29
Treatment of HIV-positive adults	30
Treatment of children	31
Special situations: pregnancy, perinatal exposure, adults with drug-resistant infection, adults with old fibrotic lesions on chest x-ray	32
Pretreatment evaluation	33
Management during treatment	35
Completion of treatment	36

Diagnosis of Tuberculosis Disease	39
Indications for collection of sputum specimens	39
Sputum specimen collection	40
Laboratory examination	41
Radiographic examinations	43
Emerging diagnostic tools	43
Tuberculosis surveillance case definition	44
Restriction of activities and uncooperative patients	45
Treatment of Tuberculosis Disease	47
Drug regimens	47
Drug resistant tuberculosis	49
Pregnancy and tuberculosis	49
Extrapulmonary tuberculosis	49
Treatment of children	50
Pretreatment evaluation and activities	50
Restriction of activities	51
Monitoring therapy	51
Non-compliant patients	52
Completion of therapy	53
Indigent patients	53
Public Health Investigations	55
Definitions	55
Objectives and priorities	55
General principals of contact and associate investigations	56
Contact selection	56
Investigation procedures	57
The “concentric circle” method	58
Treatment failure	58
Antibiotics Used to Treat Tuberculosis	59
Isoniazid	61
Rifampin	62
Pyrazinamide	63
Ethambutol	63
Streptomycin	64
Cycloserine	65
Ethionamide	65
Capreomycin	66
Para-aminosalicylic acid	66

Ciprofloxacin	67
Ofloxacin/Levofloxacin	67
Kanamycin	68
Periodic Screening for Latent Tuberculosis Infection	69
Screening of school children	69
Screening of immigrants	70
Screening of occupational and other groups	70
Institutional screening	71
The Public Health Nurse’s Role in Tuberculosis	73
Health education	73
Reporting	73
Tuberculin skin testing of school children	73
Contact and associate investigations	73
Monitoring treatment	74
Screening of clients	75
Specific activities conducted by public health nurses	75
Non-responsibilities	78
Appendix 1. Statutes and Regulations	79
Appendix 2. Forms and Instructions	97
Screening Form for Persons with a Positive Tuberculin Skin Test	98
Tuberculosis Questionnaire/Request for Chest X-Ray Interpretation	100
Drug Order and Refill Request (Form 10)	102
Record of Examination of Close Contacts of Active Cases or Associates of	104
Recent Converter (Form 43)	
Patient Surveillance Report	106
Clinical Summary/Update/Chest X-Ray Interpretation - (formerly Form 17)	108
Examination for Tuberculosis - (Form 06-1216)	109
School Tuberculin Testing Report - (Form 41)	110
Consent for Release of Medical Information	114
Hospital Discharge Plan for Patients with Tuberculosis	115
Appendix 3. Federal Guidelines for Preventing the Transmission of <u>Mycobacterium tuberculosis</u> in Health-Care Facilities, 1994	117
Appendix 4. Antibiotic Dosage Charts	121
Index	125

Preface

Tuberculosis in Alaska has declined dramatically during the past 4 decades. The incidence of tuberculosis among Alaska Natives dropped from 1,854 cases per 100,000 in 1952 to 39 cases per 100,000 in 1999. Among all Alaskans, the annual incidence in 1999 was 9.8 cases per 100,000 - 53% higher than that of the United States as a whole during 1998. The Alaska rates during 1999 among Alaska Natives and among Asians and Pacific Islanders - 39 per 100,000 and 43 per 100,000, respectively - were roughly 20 times the rate for whites (2 cases per 100,000). The high rates among Alaska Natives and Asians reflect not only the high prevalence of latent tuberculosis infection among these groups, but also the active transmission of tuberculosis, especially to children.

The goal of the Division of Public Health is to eliminate tuberculosis in Alaska.

The attainment of this difficult goal will require the cooperation and coordinated efforts of medical providers, Alaska Native Regional Health Corporations, Alaska's public health nurses, and the Tuberculosis Control Program.

The Tuberculosis Control Program is a functional component of the Section of Epidemiology. This manual has been prepared for use by Alaska health-care providers. The first section of the manual describes the Tuberculosis Control Program's strategy for the elimination of tuberculosis. The next sections contain detailed information about the pathogenesis and transmission of tuberculosis, the treatment of latent tuberculosis infection and tuberculosis disease, tuberculin skin testing, and public health investigations. The final section defines the roles and responsibilities of public health nurses in tuberculosis control.

Frequently Asked Questions

How often do cases of tuberculosis (TB) occur in Alaska?

In Alaska, on average 55 to 60 persons are reported with active TB every year. In an atypical year, up to 100 persons may be reported with TB. This is actually a small number of TB cases compared to many states, but the annual number of cases per capita for Alaska has always been higher than the national average. During 1994-1999, the rate of TB in Alaska varied from 9.0 to 16.0 cases per 100,000 population while the U.S. had a rate of 6.4 cases/100,000 in 1999. Some regions in Alaska have more TB activity: the Northern and Southwestern regions have TB rates that are 5 to 10 times higher than the State average.

How is tuberculosis (TB) spread?

TB is spread through the air on tiny particles that can remain suspended for long periods of time. A person with active, infectious TB produces these infectious particles while coughing, sneezing, laughing or singing. Close and prolonged exposure is generally required for TB to be spread. TB is not spread through food or water, by touching inanimate objects, or by exposure to blood.

What does close and prolonged exposure to tuberculosis (TB) mean?

People who are close contacts to a person with infectious TB are at highest risk for becoming infected with tubercle bacilli. These are usually people who live in the same household, work in the same workspace or otherwise spend several hours a day with the person with TB. Some persons spend more time with friends in social settings than with family, so their friends would be their close contacts.

Public health nurses do a contact investigation for each person with active TB. They ask the

person with TB who he or she spends a lot of time with. Not everyone with active TB is infectious, and doing the contact investigation helps determine the infectiousness of a TB case. Depending on the number of persons in the household or workplace who have a new positive TB skin test, the investigation may be broadened to include persons with less close contact.

What is the difference between latent tuberculosis infection (LTBI) and tuberculosis (TB) disease?

LTBI results from the slow, controlled multiplication of tubercle bacilli following inhalation of air that has been contaminated with Mycobacterium tuberculosis. Air can become contaminated when a person with active TB coughs or if M. tuberculosis organisms become aerosolized in a laboratory setting. Persons with LTBI are asymptomatic, non-infectious, and do not have chest x-ray abnormalities due to M. tuberculosis. The only method for identifying persons with LTBI is a tuberculin skin test; however, it may take up to 3 months after infection for a tuberculin skin test to become positive.

A person with LTBI will develop TB disease if the multiplication of tubercle bacilli becomes rapid and uncontrolled. Persons with TB disease are usually symptomatic and, depending on the site and severity of disease, may be infectious. About 10% of persons with LTBI will develop TB disease during their lifetime; about half of the risk is within the first 2 years after acquisition of LTBI. Persons with HIV infection and LTBI are at substantially greater risk of developing TB disease.

How can a person avoid getting tuberculosis (TB)?

Persons in close contact with someone having infectious TB may not be able to avoid becoming infected and developing latent tuberculosis infection (LTBI). However, the risk of LTBI progressing to tuberculosis disease can be reduced by proper treatment since treatment of LTBI reduces the risk of TB disease by 70% to 90%. About a third of the world's population has LTBI, making TB a major international public health problem. BCG vaccine is used in other countries even though it offers minimal protection. Other vaccines are being studied, but none appear very promising.

Are children with tuberculosis (TB) disease contagious?

Young children with TB disease are almost never contagious. Although every case must be individually evaluated, infants, toddlers and children in grades K-6 with TB disease are usually non-infectious.

Can a tuberculin skin test be placed on a patient who has previously received BCG?

Yes, a tuberculin skin test can be placed on anyone who is not already documented to have a positive result. Most persons who have received BCG vaccination are from countries with a high incidence of tuberculosis and therefore are at risk of tuberculosis. Although it is widely believed that all or most persons who have received BCG will have a reactive skin test, in reality a minority of BCG recipients have a skin test reaction ≥ 10 mm. The interpretation of skin test results for persons who have received BCG is discussed on pages 23-24.

Does a tuberculin skin test reactor (or converter) need to be excluded from school or work?

No, a positive skin test is evidence of latent tuberculosis infection, not tuberculosis disease.

Unless a person has symptoms suggesting tuberculosis disease (for example cough, fever, or weight loss) it is unnecessary to limit their usual activities. A child enrolled in school who has a positive skin test (and no symptoms of disease) can remain in school; however, the child must present within 30 days a written statement from a doctor or nurse stating that the child is not infectious to remain in school. (See page 69).

What evaluation is necessary before starting treatment of latent tuberculosis infection (LTBI)?

It is critical that all persons being treated for LTBI first have tuberculosis disease ruled-out. Thus, a chest x-ray and symptom screen must be completed before starting treatment. Since selection of an appropriate LTBI treatment regimen depends on knowing a patient's human immunodeficiency virus (HIV) antibody status, HIV testing and risk-reduction counseling is recommended for persons with HIV risk factors.

What regimens are recommended for treating latent tuberculosis infection (LTBI) in Alaska?

The American Thoracic Society and the U.S. Centers for Disease Control and Prevention have published treatment guidelines for LTBI. Their recommendations include a number of different regimens based around treatment with isoniazid, rifampin (or rifabutin), and pyrazinamide. There are several options for the length of treatment (from 2 months to 9 months) and frequency of treatment (daily or twice-weekly). The medication dose depends on the regimen being used. The only recommended option for persons <18 years of age is 9 months of isoniazid given daily or twice weekly. (See page 31).

Should a pregnant woman be given a Mantoux (PPD) skin test, started on treatment for latent tuberculosis infection (LTBI), or given a chest x-ray?

Pregnancy is never a contraindication for skin testing; therefore, if a woman needs to be skin tested, she should be tested even if she is pregnant. If a pregnant woman is found to have LTBI, treatment is indicated only if she is HIV antibody positive or believed to be recently infected. A chest x-ray (with appropriate shielding) should be obtained if the woman is a candidate for treatment of LTBI or if pulmonary tuberculosis is suspected. (See pages 32 and 49).

What is an appropriate evaluation for a patient who might have pulmonary tuberculosis?

The essential components are a Mantoux (PPD) skin test, a chest x-ray, and three sputum specimens (for acid-fast bacilli [AFB] smear and culture) collected on 3 separate days. Other procedures (bronchoscopy, collection of gastric washings, biopsy, or additional sputa) are occasionally necessary. (See pages 39-45).

What regimen is recommended for treating tuberculosis disease in Alaska?

Adults and children not suspected of having multidrug-resistant (MDR) tuberculosis should be started on four drugs: isoniazid, rifampin, pyrazinamide, and ethambutol. Treatment is generally for 6 months and may be given on a daily, biweekly, or thrice-weekly schedule. Persons for whom MDR-tuberculosis is suspected need more complex regimens and are treated for a longer duration. (See pages 47-51).

When can a person with pulmonary tuberculosis resume usual activities such as work, shopping, or travel?

As a general rule, persons newly diagnosed with tuberculosis should have their activities

restricted during the first 2 weeks of anti-tuberculosis treatment. They should not be allowed to go to work or travel by public transit (air, rail, ferry, or bus) during this time. Results of sputum smears obtained after 10 - 14 days of treatment should be used to help guide when a person can resume his or her usual activities. (See page 51).

What is directly observed therapy (DOT) and why do we use it?

Directly observed therapy (DOT) means a designated health-care provider watches the person with latent tuberculosis infection or tuberculosis (TB) disease swallow each dose of medication for the entire course of treatment. The DOT provider can assist identifying and solving problems with a treatment regimen (e.g., changing from pills to liquid) as well as help monitor for side effects. DOT is neither restrictive nor punitive. While most patients initially are reliable about taking TB medications, many forget to take all doses after a few weeks of treatment. This can result in treatment failure and drug resistance. Patients may find it very difficult to compel their child to swallow all the medication(s) for a long period. Without assistance, a 6- to 9-month course of one or more TB drugs is almost impossible to complete. Throughout the world, DOT has been proven to be the only method that effectively cures TB and controls outbreaks.

Which tuberculosis patients should be placed on directly observed therapy (DOT)?

All patients with infectious tuberculosis should be placed on DOT. Selecting only certain patients is discriminatory and implies that non-compliant patients can be accurately identified - all evidence shows that such predictions are unreliable. Ideally, as resources permit, patients being treated for extrapulmonary tuberculosis should also be placed on DOT. The Alaska TB Control Program has successfully used DOT for

more than 10 years. In outbreak situations, the TB Control Program strongly recommends DOT for persons being treated for latent tuberculosis infection, especially household contacts of an infectious case and children. (See pages 36, 47-49).

Are there side effects to taking TB medications?

Most patients can take TB medications without any problems, but occasionally a treatment regimen must be adjusted because of side effects. Patients should be observed for nausea with or without vomiting, abdominal pain, jaundice, or loss of appetite. Other less common side effects include arthralgia, gout, blood clotting problems, and changes in color vision. (See page 34).

Why are different people taking different drugs for different periods of time?

The regimens for treatment of latent tuberculosis infection (LTBI) and tuberculosis (TB) disease are different. TB disease is usually treated for 6 months, but may take longer if doses are missed or certain drugs cannot be used. Treatment of LTBI can take from 2 to 9 months.

Can an asymptomatic person with a positive PPD who has completed a regimen for treatment of latent tuberculosis infection become reinfected if exposed to someone with infectious tuberculosis?

The answer to this question appears to be "yes." Recent work suggests that exogenous reinfection can play an important role in acquisition of tuberculosis disease (N Engl J Med 1993;328:1137-44). Thus, in some circumstances (e.g., intense exposure to a strongly smear positive tuberculosis case with significant cough) it may be appropriate to treat a contact with latent tuberculosis infection even though the contact previously

completed a course of treatment for latent tuberculosis infection. (See page 57).

Why does Alaska use 5 mm and 10 mm as the cut-points for a positive PPD when 5 mm, 10 mm, and 15 mm are used in national recommendations?

Because the prevalence of latent tuberculosis infection (LTBI) in Alaska is higher than many other states, it is important that persons with LTBI be identified and, when indicated, placed on treatment to reduce the risk of disease. The Alaska cut-points are less likely to misclassify a person as PPD "negative" than the three tiered (5 mm, 10 mm, 15 mm) approach. (See pages 21-22).

In what situations is it important to do a contact or associate investigation?

Public health personnel should conduct a contact investigation for all cases of potentially infectious tuberculosis disease. Associate investigations should be done for all newly recognized PPD positive children ≤ 6 years of age. In addition, as time and resources permit, associate investigations should be done for converters ≥ 7 years of age. (See pages 55-56).

When should tuberculosis be reported?

Health-care providers and laboratories must report patients suspected or confirmed to have tuberculosis within 5 working days of being suspected or diagnosed. Reports should be made by calling 1-907-269-8000 during regular business hours. After hours, reports can be made to 1-800-478-1700; the caller will be connected to a 24 hour answering machine.

Strategy for the Elimination of Tuberculosis in Alaska

In February 1995, a U.S. Public Health Service team consisting of staff from the Centers for Disease Control and Prevention (CDC) and the Indian Health Service conducted a review of the Alaska State Tuberculosis Control Program. Their observations and recommendations were submitted to the Section of Epidemiology. The following recommendations, considered critical by the Tuberculosis Control Program, were among the more than 30 recommendations contained in the 1995 CDC report:

- All suspected or confirmed cases of tuberculosis should initially be treated with four drugs.
- The number one priority should be successful completion of treatment by persons with active tuberculosis.
- Consideration should be given to creative approaches using incentives and enablers to promote patient adherence with treatment.

Alaska Division of Public Health strategy for the elimination of tuberculosis

1. Diagnosis and treatment of all persons with pulmonary tuberculosis. These are the persons most likely to transmit infection. Prompt diagnosis and appropriate treatment of these persons are essential to limiting the spread of tuberculosis. Directly observed therapy is indicated for all persons being treated for pulmonary tuberculosis.

2. Public health investigation of close contacts of all cases of pulmonary tuberculosis. All household members residing with a case of pulmonary tuberculosis require, at a minimum, skin testing for tuberculosis infection. Those determined to have latent tuberculosis infection or to be at high risk for progression to tuberculosis disease should receive

appropriate treatment in order to reduce the risk of future tuberculosis disease.

3. Targeted skin test screening. Effective programs are needed to identify (and to treat, when appropriate) persons infected with Mycobacterium tuberculosis.

- Skin testing of schoolchildren in grades kindergarten and seven (or in a district for the first time) is required by State law.
- More extensive testing is indicated in schools with a large Alaska Native, Asian, or immigrant population or with a significant proportion of tuberculin reactors among the student population.
- Treatment of all children with latent tuberculosis infection.
- Investigation of close associates of newly infected children in order to identify the source of infection and other infected associates.
- Targeted screening of high-risk adult populations. For example, new immigrants from high-prevalence areas, Alaska Natives, and homeless or incarcerated persons.

Consistent application of the above strategy will reduce the transmission of M. tuberculosis and decrease the population of infected persons at risk of developing tuberculosis disease.

Components of Alaska's Tuberculosis Control Program

1. Tuberculosis case registry. The case registry contains data on patients with tuberculosis disease and on investigated contacts of those cases. It enables public health personnel to track diagnostic information on patients with tuberculosis and monitor their clinical management and response to therapy.

2. Provision of anti-tuberculosis drugs. The Tuberculosis Control Program supplies anti-tuberculosis medications free-of-charge for the duration of treatment to patients being treated for tuberculosis disease or latent tuberculosis infection.

3. Laboratory services. The Section of Laboratories provides laboratory services, including acid-fast bacilli smears, mycobacterial cultures, and antibiotic susceptibility testing of mycobacterial isolates.

4. Expert consultation. Physicians and other health-care providers are encouraged to consult with the Tuberculosis Control Program for questions concerning clinical diagnosis, treatment and management of tuberculosis disease, or treatment of latent tuberculosis infection.

5. Disease reporting and surveillance. The goal of surveillance is the detection of all persons with tuberculosis disease, for the dual purposes of a) treatment and control of disease; and b) program planning and evaluation, including:

- Data analysis - determination of incidence rates by age, sex, race, geographic area, and subpopulation;
- Identification of high-risk groups;
- Provision of outreach programs to persons at increased risk of developing tuberculosis disease or infection (for example, immigrants from high-prevalence countries and the urban homeless);
- Formulation of State tuberculosis control policies; and
- Evaluation of effectiveness of program activities.

6. Training. Training and education is provided to update health-care practitioners on tuberculosis diagnosis, treatment, follow-up and epidemiology in Alaska.

7. Formation of community partnerships. The Tuberculosis Control Program works closely with local agencies (such as Alaska Native health corporations) to coordinate tuberculosis control activities.

Key activities

1. Patient care. The Tuberculosis Control Program does not provide direct medical care to patients. Evaluation and treatment of patients with suspected or documented tuberculosis disease or with latent tuberculosis infection is conducted by a health-care provider of each patient's choice. The Tuberculosis Control Program will assist to assure that patients have a "medical home" to provide for their clinical needs.

2. Elimination of the use of chest x-rays for screening. Chest x-ray examinations of unselected persons have a very low yield as a screening test for tuberculosis and their routine use for such purpose is not recommended. Chest x-ray examinations should be obtained only when a specific medical indication exists (e.g., relevant history, symptoms, or candidate for treatment of latent tuberculosis infection).

The use of chest x-rays for pre-employment screening, for routine follow-up of tuberculosis patients who have completed treatment, for periodic screening in long-term care facilities, or for periodic evaluation of tuberculin reactors, should be discontinued.

As an indicator of response to tuberculosis treatment, chest x-ray examinations are less reliable than results of sputum smear and culture and assessments of symptoms and clinical status; thus, routine periodic chest x-ray examinations during treatment of tuberculosis disease are not recommended. Chest x-rays performed during initial evaluation for tuberculosis, at 2 - 3 months after initiation of treatment for tuberculosis disease, and at completion of treatment, are reasonable.

The Tuberculosis Control Program provides limited reimbursement for chest x-rays including those obtained during the course of treatment for tuberculosis disease, only if authorization for payment has been pre-approved and if the patient does not have health insurance coverage which would pay for the x-ray. If pre-approved, reimbursement is for both the chest x-ray and its interpretation. The Tuberculosis Control Program does not pay for routine chest x-rays. (See page 43).

3. Universal use of directly observed therapy. A major objective of the Tuberculosis Control Program is to assure that all patients complete recommended treatment for tuberculosis disease or latent tuberculosis infection. With the assistance of other public health personnel, the Program will monitor and encourage patient compliance with medical treatment and with clinical follow-up. **Directly observed therapy is indicated for all patients with pulmonary tuberculosis.** Incentives (for example, provision of room and board during therapy) may be needed and will be provided for patients who resist treatment or whose lifestyles make compliance with treatment regimens difficult.

4. Treatment of latent tuberculosis infection (LTBI). Certain groups of persons with LTBI are known to be at high-risk of developing tuberculosis. The benefits of treating LTBI among these persons far outweigh the risks. However, treatment of LTBI is underutilized in Alaska. **Persons for whom treatment for LTBI is recommended are as follows:**

- a. Infected household members and other infected contacts of infectious tuberculosis cases.
- b. Newly infected persons (those who developed a positive Mantoux (PPD) skin test within the past 2 years). The risk of developing disease is greatest during the first 2 years following infection.

- c. Infants, children, and adolescents ≤ 18 years of age.

- d. Persons with a positive Mantoux (PPD) skin test reaction and an abnormal chest x-ray. Treatment should be given to tuberculin skin test reactors with either radiographic findings consistent with nonprogressive (previous) tuberculosis disease (negative bacteriology and stable parenchymal lesions) or a history of previous tuberculosis that was not adequately treated. (See also pages 32-33).

- e. Persons with a positive reaction to a Mantoux (PPD) skin test and any of the following clinical conditions or treatments which are associated with an increased risk of developing tuberculosis:

- HIV antibody positive or suspected to be HIV antibody positive;
- End-stage renal disease;
- Diabetes mellitus;
- Prolonged treatment with adrenocorticosteroids;
- Immunosuppressive therapy;
- Some hematologic and reticuloendothelial diseases, such as leukemia and lymphoma;
- Silicosis;
- Clinical situations associated with substantial rapid weight loss or chronic undernutrition (e.g., intestinal bypass surgery, postgastrectomy, chronic ulcer disease, malabsorption syndrome, etc.);
- Foreign-born persons from high-prevalence countries;
- Racial and ethnic groups with higher rates of tuberculosis (e.g., Alaska Natives and Asians);

- Residents of long-term care facilities such as nursing homes, prisons, and psychiatric institutions; and
- Other persons based on clinical assessment of risk and benefit.

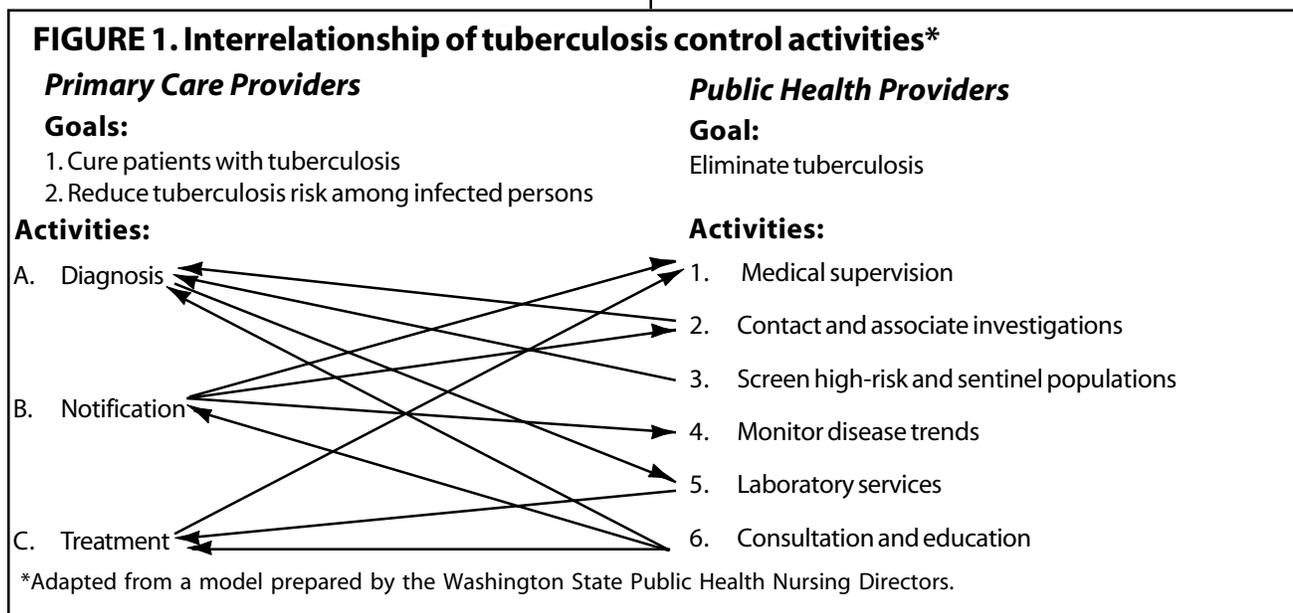
5. Increased public health investigations. Public health investigations are critical to identify likely sources of transmission and to limit the spread of tuberculosis. This is accomplished through systematic evaluation of contacts of potentially infectious cases and associates of persons with latent tuberculosis infection (see pages 55 - 58).

6. Targeted skin test screening. Testing among high risk populations can identify persons who would benefit from treatment of latent tuberculosis infection. High risk groups include recent immigrants from high-prevalence countries, homeless persons, persons with HIV infection, and others. In addition, skin testing of Alaska school children is an important tool for both identifying children in need to treatment and monitoring tuberculosis activity in the community.

7. Increased utilization of sputum specimens. Early detection of infectious pulmonary

tuberculosis can be improved by collecting sputum for acid-fast bacilli (AFB) smear and mycobacterial culture. The Tuberculosis Control Program encourages primary health-care providers (including physicians, nurse practitioners, physician assistants, and especially community health aides) to obtain three sputum specimens from any patient with a cough lasting more than 10 - 14 days, particularly if the patient has a positive Mantoux (PPD) skin test.

8. Building health-care partnerships. The effective control of tuberculosis requires that public health and primary care health providers work together to coordinate their activities. In Alaska, this means that tuberculosis control depends upon continued cooperation among a large and diverse group including: private physicians and other primary care practitioners, Alaska Native health corporations, U.S. Department of Defense health-care providers, local public health agencies, and state public health staff in the Sections of Laboratories, Public Health Nursing, and Epidemiology. There is a strong interrelationship of tuberculosis related activities between primary care and public health providers (Figure 1).



Bacteriology and Pathogenesis

Bacteriology

Tuberculosis is caused by Mycobacterium tuberculosis, a bacterium also referred to as the "tubercle bacillus." M. tuberculosis is an aerobic, nonmotile, non-spore forming organism with a multilayered cell wall rich in lipids (fats). Because of their lipid-rich walls, mycobacteria are difficult to stain. However, once they are stained, they resist decolorization with acid alcohol; hence, their designation as acid-fast bacilli or "AFB." Although all known strains of M. tuberculosis are acid-fast, there are several other acid-fast mycobacteria besides M. tuberculosis - these are often referred to as "atypical mycobacteria" or, more properly, "nontuberculous mycobacteria."

M. tuberculosis grows best at 37° C; because it grows relatively slowly, it becomes visible on solid culture media only after 3 - 6 weeks of incubation.

Transmission of tubercle bacilli

Tuberculosis is transmitted by the respiratory route: persons become infected by inhaling bacilli exhaled by persons with infectious pulmonary tuberculosis. M. tuberculosis is carried through the air in infectious droplet nuclei, which are dried, airborne residua of the large respiratory droplets discharged into the air when a person with tuberculosis of the lung or larynx sneezes, coughs, speaks, or sings. These droplet nuclei, measuring 1 - 10 microns, may remain suspended in still air for days. (Rarely, infection may result from inhalation of bacilli aerosolized from open wounds, laboratory specimens, etc. Transplacental passage, though exceedingly uncommon, can result in congenital infection.)

In contrast to large respiratory droplets, which either fall to the ground or are filtered out by the upper respiratory tract, droplet nuclei are

small enough to be inhaled directly into the lung's smallest airways (respiratory bronchioles and alveoli), where the tubercle bacilli can multiply and cause infection. Although it is possible for M. tuberculosis to invade the body directly through breaks in the mucous membranes or in the skin, this route of transmission is exceedingly rare. For all practical purposes, only persons with pulmonary or laryngeal tuberculosis should be considered capable of transmitting M. tuberculosis.

Tuberculosis is not a highly infectious disease; transmission usually requires close, frequent, and prolonged exposure. Ordinarily, even the closest household contacts of a person with pulmonary tuberculosis do not all become infected. The following factors affect the transmission of tuberculosis:

- The presence of viable bacilli in the patient's sputum;
- Sputum aerosolization as droplet nuclei when the patient coughs;
- The concentration of bacilli in the air of the host's environment;
- The susceptibility of the host; and
- The length of time the host breathes contaminated air.

The transmission of tuberculosis can be reduced or eliminated in several ways.

Ventilation with fresh air will reduce the concentration of droplet nuclei in any enclosed space. Twenty or more room air changes per hour are desirable. Room air should be exhausted to the outside and not recirculated.

The number of viable tubercle bacilli can be reduced by ultraviolet irradiation or high-efficiency particulate air (HEPA) filtration of air containing infectious droplet nuclei.

Effective anti-tuberculosis treatment reduces the number of bacilli in the air by rapidly reducing the number of organisms in a patient's sputum and the frequency of coughing.

Covering the mouth and nose with tissues while coughing or sneezing reduces the number of airborne organisms by minimizing the number of large respiratory droplets discharged into the air. A surgical mask worn by a patient is helpful in reducing the number of respiratory droplets discharged. However, **surgical masks worn by health-care workers, hospital visitors, family members, or others do not offer adequate protection** since such masks are not tight fitting and therefore do not prevent inhalation of infectious droplet nuclei.

Health-care workers who enter rooms in which patients with known or suspected infectious tuberculosis are being isolated should use a respiratory protection device capable of filtering $\geq 95\%$ of $1\mu\text{m}$ (1 micron) particles. Health-care facilities are responsible for providing acceptable respirators and assuring that they fit properly (see Appendix 3).

Methods once considered important for inhibiting transmission of tuberculosis - disposing of clothing and linens, sterilizing fomites, boiling dishes and utensils, and wearing caps, gowns, and gloves - are ineffective and unnecessary.

Pathogenesis of tuberculosis

Initial infection - Viable tubercle bacilli (in the form of droplet nuclei) which are inhaled by a susceptible host and which reach the respiratory bronchioles or alveoli are able to multiply in those sites with little or no initial resistance from the host. The organisms are slowly engulfed by macrophages, but the bacilli can remain viable within the macrophages. The tubercle bacilli gain access to lymphatic channels; they are then

distributed to regional (hilar and mediastinal) lymph nodes, and possibly to the bloodstream and to more distant sites. The bone marrow, liver, spleen, upper lung zones, renal parenchyma, epiphyseal lines of long bones, and cerebral cortex are frequently seeded with organisms.

Within 2 to 10 weeks after initial infection, the body normally is able to mount an immune response to the tubercle bacilli. The immune response is cell-mediated; it is manifested by a significant reaction to the intradermal injection of tuberculin. In most persons, this immune response prevents uncontrolled multiplication of the tubercle bacilli, and the minute lesions associated with initial infection heal, though the mycobacteria may remain viable for many years. There are no symptoms during the initial infection and if bacterial multiplication is controlled, the result is latent tuberculosis infection (LTBI). **Persons who have LTBI are not capable of transmitting tuberculosis infection to others;** transmission can occur only when a person develops tuberculosis disease.

Primary tuberculosis - A minority of persons (particularly young children and those who are immunosuppressed) develop tuberculosis disease shortly after their initial infection with M. tuberculosis because they are immunologically unable to control the multiplication of tubercle bacilli. Most persons (almost 70%) with primary tuberculosis are asymptomatic; those with symptoms may have cough, fever, weight loss, or malaise. Disease is usually confined to the thorax. A chest x-ray may show hilar or paratracheal adenopathy (90% of cases); an upper- or lower-lobe infiltrate without cavitation; atelectasis (in 30%); or pleural effusion.

Reactivation (or "adult") tuberculosis - The majority of persons develop LTBI (rather than primary tuberculosis) following an initial

infection. However, after an interval of years or decades, a small group of persons with LTBI will develop tuberculosis disease when viable organisms in an old focus of infection begin to undergo uncontrolled multiplication. The most common site in which this acceleration of growth occurs is the upper lung zone; the lungs account for the majority of clinical cases of tuberculosis today. Reactivation-type pulmonary tuberculosis is associated with abscesses which erode into the bronchi. The liquid, mycobacteria-rich contents of these abscesses are discharged into the air when the patient coughs or sneezes, resulting in airborne dissemination of infectious particles. However, foci anywhere in the body can be sites of reactivation. Extrapulmonary tuberculosis may involve any of the organs seeded with bacilli during the initial infection: bones, kidneys, lymph nodes, and the central nervous system are among the possibilities.

A person with **latent tuberculosis infection** (LTBI) is one who has a positive reaction to a Mantoux (PPD) skin test but has no clinical, bacteriologic, or x-ray evidence of tuberculosis disease.

A person is considered a **tuberculosis suspect** when the diagnosis of tuberculosis disease is being considered, whether or not treatment has been started, until diagnostic procedures have been completed.

A person with **active tuberculosis** is one who has been diagnosed as having current tuberculosis disease by bacteriologic or clinical criteria. Such a person remains "active" until treatment for the current episode of disease is completed.

Infectiousness of patients with pulmonary tuberculosis

Infectiousness of pulmonary tuberculosis patients varies considerably from case to case. In general, patients with positive acid-fast bacilli (AFB) smears are much more likely to be infectious than smear-negative patients. The conversion of a patient's AFB smears from positive to negative is an indicator of diminished infectiousness.

Riley and Moodie (Am Rev Respir Dis 1974; 110:810-2) showed that most pulmonary tuberculosis patients rapidly lose infectivity after initiation of treatment. Brooks, et al (Am Rev Respir Dis 1973; 108:799-804) showed that tuberculosis patients being treated with appropriate antimicrobials can be discharged from the hospital safely without additional risk to their close contacts. However, Clancy (Bull Int Union Tuber Lung Dis 1990; 65:70) cautioned that the belief that all patients are no longer infectious after 2 weeks of appropriate treatment has become elevated to the status of dogma. He urged a cautious approach to all patients who remain smear or culture positive no matter how long they have been treated.

The Tuberculosis Control Program considers patients who initially have one or more positive AFB smears or who have a positive culture to remain infectious until **all three** of the following conditions are met:

- The patient has completed a minimum of 14 days of adequate treatment.
- The patient has had a favorable clinical response to treatment. This could include a reduction in cough or resolution of fever.
- The patient has had three consecutive negative sputum AFB smears collected on different days.

Patients suspected to have pulmonary tuberculosis should be considered to be infectious until the patient has had three consecutive negative sputum AFB smears collected on different days.

Extrapulmonary tuberculosis

In approximately 15 - 20% of cases, tuberculosis predominantly or exclusively involves organs other than the lungs. This is the result of lymphohematogenous spread of tubercle bacilli which usually occurred years previously, at the time of initial infection with M. tuberculosis. Isolation of tubercle bacilli may not always be possible. Pulmonary tuberculosis coexists in many cases.

Pleural tuberculosis, associated with a predominantly lymphocytic exudate, is the most common form of extrapulmonary tuberculosis. Cough, fever, and pleuritic chest pain are the usual symptoms. It is probably a late manifestation of pulmonary tuberculosis and occurs when a subpleural tuberculous abscess breaks down and discharges its contents into the pleural space. Pleural tuberculosis may occur without x-ray evidence of pulmonary tuberculosis. It is best diagnosed with a pleural biopsy.

Disseminated (miliary) tuberculosis arises from hematogenous spread of tubercle bacilli, either at the time of initial tuberculosis infection or, during reactivation-type disease, when a tuberculous abscess erodes into a blood vessel. This insidious form of tuberculosis is associated with fever and nonspecific constitutional symptoms. The elderly and the very young are most often affected. It formerly was a fatal disease but now is curable if diagnosed early.

Renal tuberculosis often is asymptomatic and is suspected because of microscopic hematuria or sterile pyuria. Urine mycobacterial cultures usually are positive. **Lymphatic tuberculosis**

presents most often as a cervical or axillary mass, sometimes mildly tender (tuberculous cervical lymphadenopathy is termed scrofula). Biopsy is necessary for diagnosis. Atypical mycobacteria are frequently a cause of mycobacterial lymphadenitis. **Bone and joint tuberculosis** most often affects the lower spine, the hip, or the knee. Localized pain and swelling are the usual symptoms. **Other sites** of extrapulmonary tuberculosis include the meninges, larynx, peritoneum, pericardium, adrenal glands, genital tract, eye, and skin.

Tuberculin Skin Testing

Mycobacterial infection causes a cell-mediated immune response known as a delayed hypersensitivity reaction. The tuberculin skin test takes advantage of this immune response to identify persons who have been infected with Mycobacterium tuberculosis or other mycobacteria.

When “tuberculin” (a protein extract of M. tuberculosis) is injected into the skin, a delayed hypersensitivity reaction will be manifested as an area of induration at the injection site 48 to 72 hours following the injection. This reaction indicates that the person’s immune system “recognizes” tuberculin antigen from previous infection with M. tuberculosis or other mycobacteria. Persons who have not had previous mycobacterial infection will not show this immune response and will not develop an area of induration.

Persons who have had infection with other mycobacteria may have cross-reactions with tuberculin. These cross-reactions generally result in a smaller area of induration. As a rule, the larger the reaction to tuberculin, the greater the probability that the reaction is due to M. tuberculosis. Unfortunately, like many clinical tests, tuberculin skin testing is an imperfect tool. Some persons who have been infected by other mycobacteria, but not by M. tuberculosis, will have a tuberculin skin test reaction that is classified as positive.

Conversely, 20% of persons with **untreated** tuberculosis disease may have a negative skin test (after several months of treatment, their skin test will become positive). Thus, clinical judgment plays an important role in interpreting the result of a tuberculin skin test.

Skin testing can be performed on a person of any age. Older persons are subject to waning immunity and may fail to respond to a tuberculin skin test although they actually are

infected (see “The booster phenomenon,” pages 24-25). Infants <6 months of age may not have a sufficiently developed cell-mediated immune response to be able to mount a significant reaction to tuberculin. Thus, when testing of an infant is indicated (e.g., when an infant is a household contact of an active case), the child can be skin tested at 4 - 6 weeks and, if negative, retested at 3 - 4 months and 6 months of age.

A positive reaction to a tuberculin skin test indicates, at a minimum, the presence of latent tuberculosis infection (LTBI) but does not, in itself, signify disease. Since persons who have LTBI are not infectious to others, **it is not appropriate to exclude a child from school or an adult from work or travel if the person has a positive skin test but no symptoms suggesting tuberculosis disease.** Tuberculin skin testing is a diagnostic aid in the evaluation of individual patients. It is useful for determining the prevalence of tuberculosis infection in populations and in detecting LTBI in individual members of the population. It can be especially valuable when it is repeated periodically in the surveillance of tuberculin-negative persons likely to be exposed to tuberculosis.

In general, it is useful to consider skin testing to be a first step toward treatment of possible latent tuberculosis infection (LTBI). This means there is little justification for skin testing a patient who will not be treated for LTBI if the test is positive. **A decision to skin test should be a commitment to treat.** Evaluation of symptomatic patients, public health contact (and associate) investigations, and required skin testing activities (school children, health-care workers, etc.) are obvious exceptions to this concept.

The Mantoux skin test

The Mantoux test is the test recommended by the Tuberculosis Control Program for definitive, standardized tuberculin skin testing. Whereas multiple-puncture tuberculin skin tests deposit a variable amount of antigen in the skin, the Mantoux test is based on the intradermal injection of a standard (measured) amount of tuberculin antigen. The reaction to the antigen can be measured and the result used to assess the likelihood of infection with *M. tuberculosis*. The Mantoux test is often referred to simply as a "PPD."

The Mantoux test uses PPD-S (purified protein derivative stabilized with Tween 80). PPD-S is a protein extract of the cell wall of tubercle bacilli which is stabilized with a detergent to reduce the extract's adsorption to glass and plastic. PPD-S should be used in 5-TU (five tuberculin unit) strength. PPD-S tuberculin is produced commercially in liquid form; by mid-1973 all commercially prepared PPD-S products in the United States were required to be of uniform potency and stability. A test dose of 0.1 mL is equivalent to 5 tuberculin units (TU) of PPD-S.

Persons suspected to have tuberculosis should be given a Mantoux skin test (unless they are already known to be skin test positive).

Contacts of active tuberculosis cases must be evaluated with a Mantoux test rather than with a multiple-puncture test. Anytime a patient has a positive reaction to a multiple-puncture test (multiple-puncture tests are not recommended by the Tuberculosis Control Program), the result should be confirmed with a Mantoux test.

PPD-S vials should be stored in a refrigerator at 2° - 8° C (36° - 46° F) when not in use. PPD-S should not be exposed to sunlight or strong daylight. If protected from heat, light, and contamination, unopened vials can be considered potent until the expiration date.

Potency and stability are not affected by freezing or by storage for up to 1 week at room temperature. Outdated vials should be discarded; incineration or other special handling is not necessary.

A vial of PPD-S solution which has been opened should be discarded after 1 month because oxidation and degradation may have reduced its potency. Since PPD-S tuberculin has an affinity for glass and plastic, it should not be transferred to other containers. Skin tests should be given within 2 hours after a syringe is filled.

Standard technique for intradermal application of the Mantoux test:

1. Cleanse the skin with acetone or alcohol and allow to dry. Use a plastic or glass tuberculin syringe with a short (1/2 inch), bluntly beveled 26- or 27-gauge needle. Syringes may be pre-filled but should be used within 2 hours of being filled in order to reduce the risk of bacterial contamination.
2. Inject intradermally 0.1 mL of PPD-S into the skin of the volar (inner) surface of the forearm. In the interest of consistency, the left forearm should ordinarily be used. The needle tip should be advanced so that the bevel is 2 - 4 mm beyond the point of entry. The needle must be angled almost parallel to the skin surface to prevent subcutaneous injection.
3. Inject just beneath the surface of the skin with the needle bevel upward so that a 6 mm to 10 mm wheal is produced. If the needle goes beyond the intradermal area, do not inject subcutaneously. Withdraw from the subcutaneous area and slide the needle into the intradermal area.
4. In the event the injection is delivered subcutaneously (i.e., no wheal or bleb forms), start with a new sterile syringe and repeat the injection at another site at least 2 inches away. Read only the second intradermal injection. Do

not attempt to test more than twice if any solution has been injected subcutaneously; instead, retest in 1 month. There is no need to repeat the injection if a small amount (less than half the volume) of the PPD solution is lost outside the skin.

5. If no wheal or bleb is produced, the test should be disregarded and not interpreted. If subcutaneous injection occurs, a local reaction may develop that cannot be accurately measured.

Read the Mantoux test 48 - 72 hours after application. The reading should always be done by a health-care worker, never by the patient or a parent. An occasional patient will have an induration reaction beyond 72 hours; if this occurs, the reaction should be measured and recorded. If a patient fails to show up for reading, it is acceptable to read the result for up to 1 week after testing if the result is "positive" (as defined below). Any patient who does not return to have their skin test read at 48 - 72 hours and who has a result at 4 - 7 days which would be classified as negative should be retested.

Measure the diameter of induration (hardness) in millimeters; record the longest measurement obtained. **Erythema without induration should be considered 0 mm.** If there is erythema greater than 10 mm and induration is absent, the injection may have been made too deeply, and retesting is indicated. Do not attempt to test more than twice in 1 month if the injection has been administered subcutaneously.

Interpreting the Mantoux skin test

Latent tuberculosis infection (LTBI) is diagnosed whenever a person has a "positive" Mantoux (PPD) skin test, as defined below, and no symptoms of tuberculosis disease. Selection of patients with LTBI for treatment is described in the next chapter.

A **tuberculin converter** is a person whose reaction to a Mantoux (PPD) skin test has increased by at least 10 mm, from <10 mm to 10 mm or more, within the preceding 24 months. In order to be classified as a converter, each of three essential characteristics must be met: (1) the PPD must have increased by at least 10 mm; (2) the increase must have been from <10 mm of induration to 10 mm or more of induration; and (3) the increase occurred over a time period of 24 months (or less).

A **tuberculin reactor** is a person with a positive tuberculin reaction, as defined below, whose tuberculin skin test reaction has not been documented to "convert" (i.e., increase by at least 10 mm, from <10 mm to \geq 10 mm, within the preceding 24 months).

- Induration reactions of \geq 10 mm are considered "positive" (or "significant") for all persons.
- Induration reactions of \geq 5 mm are considered "positive" for:
 - a) Persons with human immunodeficiency virus (HIV) infection,
 - b) Close contacts of persons with newly diagnosed infectious tuberculosis,
 - c) Persons with abnormal chest x-rays showing fibrotic lesions likely to represent old healed tuberculosis,
 - d) Patients with organ transplants and other immunosuppressed patients (receiving the equivalent of \geq 15 mg/d of prednisone for 1 month or more), and
 - e) Patients with abnormal chest x-rays consistent with active pulmonary tuberculosis.
- Induration reactions of 0 - 4 mm are considered "negative" for all persons.

The 5 mm and 10 mm cut-points described above differ from the 5 mm, 10 mm, and 15 mm cut-points recommended by the U.S. Centers

for Disease Control and Prevention (CDC), the American Thoracic Society, and the American Academy of Pediatrics. The Alaska Tuberculosis Control Program uses the 5 mm and 10 mm cut-points for the following reasons:

- This classification scheme is more conservative; i.e., persons who have a 10 - 14 mm Mantoux skin test and who would be classified as “negative” by the three tiered (CDC) criteria will be classified as “positive” by the Alaska criteria. It is appropriate to consider such persons to have tuberculosis infection since Alaska has a higher prevalence of tuberculosis infection than other states.
- The scheme is simpler to apply and less likely to result in misclassification. The experience of the Tuberculosis Control Program is that clinicians have difficulty applying the three tiered CDC criteria unless it is used on a frequent basis. Patients with a 10 - 14 mm PPD who have risk factors for tuberculosis infection (and would be properly classified as “positive” by the CDC scheme) might be misclassified as having a negative skin test if a careful and detailed history is not taken or if the three tiered criteria are not fully understood.

An earlier edition of the *Alaska Tuberculosis Policy Manual* mentioned a so-called “doubtful reaction” (i.e., a Mantoux skin test of 5 - 9 mm in a person for whom such a result would be classified as negative). Mantoux skin test results of 5 - 9 mm are no longer classified as “doubtful” and do not need to be repeated unless either the patient is being tested using a two-step procedure (described below, pages 24-25) or there is uncertainty concerning the size of the indurated area (e.g., no clear margin is palpable). A 5 - 9 mm Mantoux result should be classified as “positive” or “negative” based on the criteria described above.

Multiple-puncture skin tests

Multiple-puncture tests (e.g., Tine, Mono-Vacc, Aplitest) use concentrated tuberculin and are not standardized in humans. In addition, the amount of tuberculin introduced into the skin using the multiple-puncture technique cannot be controlled. The Tuberculosis Control Program does not recommend the use of multiple-puncture tests; any positive result should be followed-up with a Mantoux (PPD) test unless the multiple-puncture test causes vesiculation. In this case, the test can be considered “positive” and a Mantoux does not need to be placed. **Decisions concerning individual patient management should never be made on the basis of a response to a multiple-puncture test.**

Multiple-puncture tests are not intended for diagnostic use in suspected tuberculosis cases or in contacts of active tuberculosis cases. They have been used for surveys or screening among groups of asymptomatic persons not exposed to a case of tuberculosis in whom only a small proportion are expected to have tuberculosis infection. The Tuberculosis Control Program no longer supplies multiple-puncture tests.

False negative skin tests

Persons infected with *M. tuberculosis* usually develop the ability to react to a tuberculin skin test 2 to 10 weeks following infection. A skin test reaction may be negative, despite the presence of infection, in the following circumstances:

1. Early tuberculosis infection: Delayed hypersensitivity may not yet have developed.
2. Active tuberculosis disease: Approximately 20% of patients with newly diagnosed pulmonary tuberculosis will have a negative reaction to a Mantoux skin test. An even higher percentage of patients with overwhelming tuberculosis disease (miliary tuberculosis) will

have a negative skin test, compared with a lower percentage of patients with other forms of extrapulmonary tuberculosis. Persons with active tuberculosis who have a negative skin test will usually become skin test positive after 2 or 3 months of anti-tuberculosis treatment.

3. Advancing age: As people grow older, immune responsiveness decreases. As a result, some persons who were infected with M. tuberculosis many years previously may have a false negative skin test. Many of these people demonstrate the booster phenomenon if retested (see page 24).

4. Very young age: Infants <6 months of age may not have a sufficiently developed cell-mediated immune response to be able to mount a significant reaction to a tuberculin skin test. If testing is indicated, an infant should be skin tested at 4 - 6 weeks, and if negative, retested at 3 - 4 months and 6 months of age.

5. Viral infection or vaccination with a live virus: Occasionally following a severe viral infection or a live-virus vaccination, a person with M. tuberculosis infection may be temporarily unable to respond to a tuberculin skin test. A negative Mantoux should be repeated in 6 weeks following severe viral illness. A tuberculin skin test can be given either on the same day that a live-virus vaccine (measles, mumps, rubella, varicella, yellow fever vaccine, or oral polio) is administered or ≥ 4 weeks afterwards. Persons with typical mild or moderate upper respiratory symptoms are unlikely to be anergic and can be skin tested.

6. Immunosuppression: Persons who have anergy due to serious illness (e.g., AIDS, cancer, sarcoidosis), or are receiving adrenocorticosteroids, cancer chemotherapy, or other immunosuppressive drugs may not be able to mount an immune response to a tuberculin skin test. Steroid inhalers used to treat asthma do not contain a large enough steroid dose to cause immunosuppression.

7. Malnutrition.

8. Idiopathic: Up to 5% of otherwise healthy persons infected with M. tuberculosis may have a negative tuberculin skin test.

BCG vaccine

Bacillus Calmette-Guérin (BCG) vaccine, derived from an attenuated strain of M. bovis, is used in many parts of the world to immunize persons against M. tuberculosis. The vaccine is used primarily in areas with high prevalence rates of tuberculosis; the efficacy of different strains of the vaccine varies widely. One problem with BCG vaccine is that it induces sensitivity to tuberculin in some persons who receive it. Thus, after BCG vaccination, there is no reliable method for distinguishing between a tuberculin skin test reaction caused by M. tuberculosis infection or by vaccination itself.

Undoubtedly, a positive skin test in a BCG recipient should be attributed to tuberculosis infection if the patient either has risk factors for tuberculosis infection or medical conditions that increase the likelihood of infection progressing to disease (Table 1). Since the great majority of BCG recipients are from countries with a high prevalence of tuberculosis, it is generally prudent to consider a positive skin test reaction in a BCG recipient to be caused by M. tuberculosis infection rather than BCG [MMWR 2000; 49(RR-6):25]. This leads to the recommendation that **previous BCG vaccination should be ignored when interpreting a tuberculin skin test.**

Occasionally, a patient with a positive skin test who received BCG will be found to have no risk factors for tuberculosis infection or disease (Table 1). In this uncommon situation, the health-care provider may think about attributing a positive skin test to BCG rather than tuberculosis infection. Before making this decision, it is important to consider:

TABLE 1. Risk factors for acquisition of latent tuberculosis infection (LTBI) or for progression of LTBI to active tuberculosis

<ul style="list-style-type: none"> • Contact of patient with tuberculosis disease • Skin test converter • Patient with fibrotic changes on chest x-ray consistent with prior tuberculosis • Human immunodeficiency virus (HIV) infection • Patient with organ transplants or immunosuppression (receiving the equivalent of ≥ 15 mg/d of prednisone for 1 month or more) • Foreign-born person from high prevalence country 	<ul style="list-style-type: none"> • Injection drug user • Resident or employee of: prison, jail, long-term care facility, hospital, health-care facility, residential facility for persons with HIV infection, homeless shelter • Mycobacteriology laboratory personnel • Person with any of the following conditions: silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, weight loss of $\geq 10\%$ of ideal body weight, gastrectomy, jejunioileal bypass, or carcinoma of the head, neck, or lung • Alaska Native or Asian • Infant or child <18 years of age
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1. Since BCG generally does not cause skin test reactions >15 mm, reactions of this size should not be attributed to BCG (MMWR 1988; 37:663-4, 669-75. JAMA 1985; 253:3438-9. Clin Infect Dis 1993; 17:968-75).

2. If a risk factor for tuberculosis infection or disease was overlooked (Table 1), the patient may benefit from treatment of LTBI but no treatment will be recommended.

BCG vaccination is not a contraindication for tuberculin skin testing. All persons who are not documented tuberculin reactors and for whom skin testing is indicated, should receive a tuberculin skin test, whether or not they have a history of BCG vaccination.

The booster phenomenon

Repeat skin testing of uninfected persons does not sensitize them to tuberculin.

However, delayed hypersensitivity to tuberculin, once it has been established by infection with any species of mycobacteria or by BCG vaccination, may gradually wane.

When skin tested many years after sensitization, some persons may have negative reactions. The stimulus of skin testing itself may then boost or increase the size of the reaction to a subsequent test, sometimes causing an apparent conversion or development of sensitivity. The booster effect can be seen on a second test done as soon as a week after the initial stimulating test and can persist for a year and perhaps longer. The prevalence of the booster phenomenon among persons who have mycobacterial infection increases with age (1.3% at ages 20 - 25 years; 4% at ages 35 - 39 years; 7% among persons over age 50 years).

When tuberculin skin testing of adults is to be repeated periodically (e.g., residents of long-term care facilities such as nursing homes; health-care workers; inmates of long-term correctional facilities), the use of two-step testing initially can reduce the likelihood of misinterpreting a boosted reaction as representing recent infection. Any adult who will be subject to periodic repeat skin testing

who does not have a documented negative skin test within the previous 12 months should be tested by the two-step method. Since persons being tested as part of a contact investigation (around a case of infectious tuberculosis) were recently exposed to tuberculosis, there is no need for two-step testing of contacts. The recommended method of two-step testing is as follows:

1. If the reaction to the first test is classified as negative, a second test should be applied 1 - 3 weeks later (see page 21).
2. If the reaction to the second of the initial two tests is ≥ 10 mm of induration, this represents a boosted reaction. Based on this second test, the person should be classified as having a positive PPD reaction and managed accordingly.
3. If the second test result remains below the cut-point (5 mm or 10 mm of induration, as described on page 21), the person is classified as having a negative reaction. A positive reaction to a third test given at a later date, is likely to represent infection with M. tuberculosis during the interval.

Adverse reactions

In highly sensitive individuals, strongly significant reactions including vesiculation, ulceration, or necrosis may occur at the test site. Cold packs may be used for symptomatic relief of pain, pruritus, and discomfort. If a severe local reaction occurs, a topical corticosteroid may be helpful. For reactions progressing to necrosis, a short course of an oral corticosteroid may be indicated. Strongly significant reactions may result in scarring at the test site.

Contraindications

There are no contraindications to the administration of commercial tuberculin preparations. Tuberculin should not be administered to persons who are documented tuberculin reactors. However, if a person's skin test history is uncertain, it is almost always best to test them. There is no contraindication to the tuberculin skin testing of pregnant women (Am Rev Respir Dis 1985; 131:809-10) or of persons who have previously received BCG vaccine. Persons with dermatitis on one forearm should be tested on the other side. Persons who have recently received a live-virus vaccine (measles, mumps, rubella, varicella, yellow fever, or oral polio) can be skin tested. However, if the result is classified as negative, it will be necessary to repeat the skin test at least 4 weeks after the live virus vaccine was administered.

Anergy testing

The term anergic is used to describe persons who are immunologically unable to respond to antigens to which they have been previously sensitized. There are numerous recognized causes of anergy such as increasing age, cachexia, acute viral infections including measles and influenza, and immune compromising conditions such as human immunodeficiency virus (HIV) infection. Because persons who are co-infected with HIV and M. tuberculosis are at extraordinarily high risk of developing active tuberculosis, in 1991 the CDC recommended that Mantoux skin test negative persons who were HIV positive be anergy tested [MMWR 1991;40(RR-5):27-33]. The CDC recommendations were based on the assumption that anergy testing would help to clarify the interpretation of a negative Mantoux result.

After publication of the CDC guidelines, anergy testing of HIV-positive, skin test negative persons became more common and its use was

recommended by the Tuberculosis Control Program (Epidemiology Bulletin 1992; No. 20). Unfortunately, the majority of HIV-positive persons who were Mantoux negative were also non-reactive to antigens on an anergy panel (Am J Respir Crit Care Med 1994; 149:1699-709). Furthermore, among elderly patients with culture confirmed tuberculosis, many who were Mantoux negative had a positive response to one or more antigens on an anergy panel (Infectious Diseases in the Elderly. Year Book Medical Publishers, Inc; 1990. 1-5). In addition, anergy panel antigens, doses, and skin test response interpretations have not been standardized.

For the above reasons, **anergy testing is no longer considered part of the clinical evaluation of immunosuppressed patients.**

One report concluded, "...any combination of skin test antigens ... will not, and cannot, lead to a substantial improvement in interpretation of a properly applied tuberculin skin test" (Am J Respir Crit Care Med 1994; 149:1699-709). The Tuberculosis Control Program does not recommend that anergy testing be included in the diagnostic evaluation of HIV-positive, tuberculin skin test-negative patients and no longer supplies antigens for anergy testing. In 1999, the CDC withdrew the recommendation to anergy test HIV-positive, PPD-negative persons (Am J Respir Crit Care Med 2000; 161:1376-1395).

Treatment of Latent Tuberculosis Infection

Treatment of latent tuberculosis infection (LTBI) with isoniazid (or other drugs) presumably acts by diminishing the bacterial population in “healed,” radiographically stable lesions, or in tiny granulomatous lesions too small to be seen on chest x-ray. A 6-month course of isoniazid reduced the incidence of tuberculosis by 69% among tuberculin reactors with fibrotic pulmonary lesions; a 1-year course reduced the incidence by 93% [MMWR 2000; 49(RR-6):1-51]. Although a 9-month regimen of isoniazid is the preferred treatment for LTBI, a 6-month regimen is an acceptable alternative (Am J Respir Crit Care Med 2000; 161:S221-47). Other treatment options are described below. The therapeutic effect of isoniazid prophylaxis has been shown to persist for at least 30 years (JAMA 1984; 251:1283-5), and it is presumed to endure for the lifetime of the treated patient.

Persons for whom treatment of latent tuberculosis infection (LTBI) is recommended

1. *The following persons should be evaluated for LTBI treatment **irrespective of their Mantoux (PPD) test results (Table 2):***

- Recent contacts <5 years of age.
- Recent contacts who are HIV-infected or immunosuppressed.

Contacts who are immunosuppressed or who have HIV infection should complete a full regimen for treatment of LTBI, irrespective of follow-up skin test results. LTBI treatment of skin-test negative children <5 years of age can be stopped if a follow-up skin-test performed at 3 (or more) months after exposure has ended is negative.

2. *The following persons should be evaluated for LTBI treatment **if their Mantoux (PPD) test is ≥ 5 mm (Table 2):***

- Persons with documented human immunodeficiency virus (HIV) infection or persons with risk factors for HIV whose HIV infection status is unknown but who are suspected of having HIV infection. In addition, persons with HIV infection or immunosuppression who have been close contacts of infectious tuberculosis are candidates for treatment of LTBI irrespective of their Mantoux test results.
- Household members and other close contacts of persons with newly diagnosed infectious tuberculosis. In addition, tuberculin-negative (i.e., Mantoux <5 mm) children <5 years of age who have been close contacts of infectious persons within the past 3 months are candidates for LTBI treatment until being re-evaluated with a repeat tuberculin skin test 3 months after contact with the infectious source.
- Persons with an abnormal chest x-ray with fibrotic lesions likely to represent old healed (untreated) tuberculosis.
- Persons with a history of tuberculosis disease that was not adequately treated.
- Persons with silicosis who have negative acid-fast bacilli (AFB) smears and mycobacterial cultures.
- Patients with organ transplants and other immunosuppressive conditions (e.g., persons receiving the equivalent of ≥ 15 mg/d of prednisone for 1 month or more).

3. The following persons should be evaluated for LTBI treatment **if their Mantoux (PPD) test is ≥ 10 mm (Table 2):**

- Infants, children, and adolescents <18 years of age.
- Tuberculin converters (documented ≥ 10 mm increase in Mantoux from <10 mm within a 2 year period).
- Persons with medical conditions which increase the risk of LTBI progressing to active tuberculosis:
 - a. End-stage renal disease;
 - b. Diabetes mellitus, especially if poorly-controlled, insulin-dependent;
 - c. Leukemia or lymphoma;

d. Clinical situations associated with substantial, rapid weight loss or chronic undernutrition (postgastrectomy, jejunoileal bypass, chronic malabsorption, etc.);

e. Intravenous drug users known to be HIV-seronegative.

- Foreign-born persons from high-prevalence countries.
- Racial and ethnic groups with higher rates of tuberculosis (e.g., Alaska Natives and Asians).
- Residents of facilities for long-term care such as correctional institutions, nursing homes, and psychiatric institutions.
- Other persons based on clinical assessment of risk and benefit.

TABLE 2. Guidelines for selection of patients for treatment of latent tuberculosis infection, by Mantoux (PPD) test result

Consider treating irrespective of PPD	Consider treating if PPD is >5 mm	Consider treating if PPD is ≥ 10 mm
<ul style="list-style-type: none"> • Recent contacts <5 years of age • Recent contacts with immunosuppression or HIV infection 	<ul style="list-style-type: none"> • All persons in the first column • Persons with documented HIV infection • Household members and other close contacts of newly diagnosed infectious tuberculosis • Persons with an abnormal chest x-ray with fibrotic lesions likely to represent old healed (untreated) tuberculosis • Persons with a history of tuberculosis that was not adequately treated • Persons with silicosis • Patients with organ transplants and other immunocompromising conditions 	<ul style="list-style-type: none"> • All persons in the first two columns • Infants, children, and adolescents <18 years of age • Skin test converters • Persons with medical conditions which increase the risk of latent tuberculosis infection progressing to active disease* • Foreign-born persons from high prevalence countries • Racial and ethnic groups with higher rates of tuberculosis (e.g., Alaska Natives and Asians) • Residents of congregate living facilities (jails, long-term care, etc.) • Other persons based on clinical assessment of risk and benefit

*See text for list of medical conditions which increase the risk of latent infection progressing to active disease.

Fundamentals of treatment for latent tuberculosis infection

For many years, isoniazid was the mainstay drug for the treatment of latent tuberculosis infection (LTBI). In April 2000, the U.S. Centers for Disease Control and Prevention (CDC) and the American Thoracic Society (ATS) jointly published a statement containing new recommendations for the treatment of LTBI [MMWR 2000; 49(RR-6):1-51].

For children <18 years of age with LTBI (not believed to be due to infection by a drug resistant strain), the CDC/ATS recommended treatment with daily or twice weekly isoniazid for 9 months. For persons \geq 18 years of age with LTBI (not believed to be due to infection by a drug resistant strain), the CDC/ATS statement included 10 possible treatment regimens (Table 3).

Based on a careful review of a number of drug efficacy studies, regimens were classified as either “preferred,” “alternate,” or “back-up” for HIV-positive or HIV-negative persons.¹ Specific treatment regimens for adults with or without HIV infection, children, and special situations (pregnancy, drug resistance, or persons with a chest x-ray with old fibrotic lesions) are discussed on the following pages.

Treatment of HIV-negative adults

For treatment of HIV-negative adults (\geq 18 years of age) with latent tuberculosis infection (LTBI) presumed to be due to isoniazid-sensitive organisms, the preferred CDC/ATS regimen is:

- 9 months of isoniazid daily at a dose of 5 mg/kg (up to 300 mg/kg).

1. The CDC/ATS statement used somewhat different terminology for classifying treatment options. However, staff at the Tuberculosis Control Program considered the above terms easier to understand and less likely to cause confusion than the CDC/ATS terms.

The CDC/ATS recommendations list five alternate regimens (Table 3):

- 9 months of isoniazid twice weekly at a dose of 15 mg/kg (up to 900 mg),
- 6 months of isoniazid daily at a dose of 5 mg/kg (up to 300 mg),
- 6 months of isoniazid twice weekly at a dose of 15 mg/kg (up to 900 mg),
- 4 months of rifampin daily at a dose of 10 mg/kg (up to 600 mg), or
- 2 months of rifampin daily at a dose of 10 mg/kg (up to 600 mg) *plus* pyrazinamide daily at a dose of 15-20 mg/kg (up to 2 gm).

If none of the above “preferred” or “alternate” regimens can be given, a back-up regimen is available (Table 3):

- 2 – 3 months of rifampin twice weekly at a dose of 10 mg/kg (up to 600 mg) *plus* pyrazinamide twice weekly at a dose of 50 mg/kg (up to 4 gm).

Regimens given on a twice weekly basis should be administered as directly observed therapy (see page 36). Because several regimens are available to treat LTBI, health-care providers should discuss options with the patient and, when possible, help patients make the decision, unless medical considerations dictate a certain regimen. Furthermore, based on patient and local considerations, some health-care providers may determine that a 6 month regimen using isoniazid is more likely to be successful than the 9 month isoniazid regimens. For treatment of HIV-negative adults with LTBI believed to be due to a drug resistant organism, see page 32.

Treatment of HIV-positive adults

For treatment of HIV-positive adults (≥18 years of age) with latent tuberculosis infection (LTBI) presumed to be due to isoniazid-sensitive organisms, there are two regimens rated as “preferred” by CDC/ATS (Table 3):

- 9 months of isoniazid daily at a dose of 5 mg/kg (up to 300 mg), or
- 2 months of rifampin daily at a dose of 10 mg/kg (up to 600 mg) *plus* pyrazinamide daily at a dose of 15-20 mg/kg (up to 2 g).

The CDC/ATS lists two alternate regimens (Table 3):

- 9 months of isoniazid twice weekly at a dose of 15 mg/kg (up to 900 mg), or
- 4 months of rifampin daily at a dose of 10 mg/kg (up to 600 mg).

If none of the above “preferred” or “alternate” regimens can be given, three back-up regimens are available (Table 3):

- 2 – 3 months of rifampin twice weekly at a dose of 10 mg/kg (up to 600 mg) *plus* pyrazinamide twice weekly at a dose of 50 mg/kg (up to 4 g).
- 6 months of isoniazid daily at dose of 5 mg/kg (up to 300 mg), or
- 6 months of isoniazid twice weekly at a dose of 15 mg/kg (up to 900 mg).

TABLE 3. Preferred, alternate, and back-up regimens for treatment of adults with latent tuberculosis infection, by human immunodeficiency virus (HIV) antibody status¹

A. Preferred regimens

Medication	Interval and Duration	Dose (mg/kg)	HIV status ²
Isoniazid	Daily for 9 months	5 (max. 300 mg)	- or +
Rifampin (RIF) <i>plus</i> pyrazinamide (PZA)	Daily for 2 months	RIF 10 (max. 600 mg) <i>plus</i> PZA 15-20 (max. 2 g)	+ ³

B. Alternate regimens

Medication	Interval and Duration	Dose (mg/kg)	HIV status ²
Isoniazid	Twice weekly for 9 months ⁴	15 (max. 900 mg)	- or + ³
Isoniazid	Daily for 6 months	5 (max 300 mg)	-
Isoniazid	Twice weekly for 6 months ⁴	15 (max. 900 mg)	-
Rifampin	Daily for 4 months	10 (max. 600 mg)	- or + ³
Rifampin (RIF) <i>plus</i> pyrazinamide (PZA)	Daily for 2 months	RIF 10 (max. 600 mg) <i>plus</i> PZA 15-20 (max. 2 g)	-

C. Back-up regimens - to be used only if preferred and alternate regimens cannot be given

Medication	Interval and Duration	Dose (mg/kg)	HIV status ²
Rifampin (RIF) <i>plus</i> pyrazinamide (PZA)	Twice weekly for 2-3 months ⁴	RIF 10 (max. 600 mg) <i>plus</i> PZA 50 (max. 4 g)	- or + ³
Isoniazid	Daily for 6 months	5 (max. 300 mg)	+
Isoniazid	Twice weekly for 6 months ⁴	15 (max. 900 mg)	+

Notes:

1. Adapted from: MMWR 2000; 49(RR-6):31.
2. For HIV status, + indicates a regimen that is suitable for HIV-positive adults and - indicates a regimen is suitable for HIV-negative adults (and persons of unknown HIV antibody status who do not have risk factors for HIV infection).
3. Rifabutin should be substituted for rifampin when treating an HIV-positive patient receiving protease inhibitors (see text, page 31).
4. Any regimen given on a twice weekly basis should be administered *only* as directly observed therapy.

Regimens given on a twice weekly basis should be administered as directly observed therapy (see page 36). Because several regimens are available to treat LTBI, health-care providers should discuss options with the patient and, when possible, help patients make the decision, unless medical considerations dictate a certain regimen. For treatment of HIV-positive adults with LTBI believed to be due to a drug resistant organism, see page 32.

Rifampin is generally contraindicated or should be used with caution in patients who are taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Rifabutin should be substituted for rifampin in patients taking indinavir, nelfinavir, amprenavir, ritonavir, or efavirenz. Caution is advised if rifabutin is administered with soft-gel saquinavir or nevirapine. Additional details, including possible dosage adjustments can be found in the CDC/ATS statement [MMWR 2000; 49(RR-6):1-51].

HIV-positive or immunosuppressed persons (of any age) who are close contacts to infectious tuberculosis should be evaluated for LTBI treatment, irrespective of the initial skin test result. If the contact has no evidence of tuberculosis disease, treatment for LTBI is indicated. The regimen should be continued until completed, even if the contact remains skin test negative (e.g., <5 mm).

Treatment of children

For treatment of children <18 years of age with latent tuberculosis infection (LTBI) presumed to be due to isoniazid-sensitive organisms, the preferred CDC/ATS regimen is daily isoniazid at a dose of 10-20 mg/kg (up to 300 mg/kg) for 9 months. As an alternate to this regimen, children may be treated with twice-weekly isoniazid at a dose of 20-40 mg/kg (up to 900 mg) for 9 months. The twice-weekly regimen, if used, should be administered as directly observed therapy (see page 36).

As of early-2001, no studies have been published examining treatment options for LTBI in children with HIV infection. The American Academy of Pediatrics recommends that one of the above two regimens be used.

If a child cannot tolerate isoniazid or is believed to be infected with an isoniazid resistant strain, the commonest choice is to treat with rifampin using a daily dose of 10-20 mg/kg (up to 600 mg). Although no duration of treatment has been established from clinical trial data, the American Academy of Pediatrics recommends 6 months.

Children believed to be infected with isoniazid-resistant or rifampin-resistant organisms are unlikely to benefit from treatment with these drugs. When possible, a regimen should be selected based upon susceptibility testing of the isolate to which the child was exposed. For children believed to have multidrug resistant LTBI, the combination of pyrazinamide (15-20 mg/kg, maximum 2 gm) and ethambutol (15 mg/kg) given daily for 9-12 months should be used if the isolate is sensitive to both drugs. When this regimen cannot be used, many experts recommend using two other drugs to which the organism is susceptible.

Special considerations are needed for close contacts of a person with infectious tuberculosis. If the contact is a child <5 years of age or is HIV-positive or immunosuppressed (at any age), the person should be evaluated for LTBI treatment, irrespective of the initial skin-test result. If there is no evidence of tuberculosis disease, treatment of LTBI is indicated. If the immune competent child's skin-test remains negative (e.g., <5 mm) when re-tested at 3 (or more) months after exposure has ended, LTBI treatment can be stopped. If the contact is immunosuppressed, the regimen should be continued to completion, even if the contact remains skin-test negative.

Special situations: pregnancy, perinatal exposure, adults with drug-resistant infection, adults with old fibrotic lesions on chest x-ray

1. Pregnancy. No harmful effects of isoniazid on the fetus have been observed and pregnancy should not be an impediment to the use of isoniazid in women with tuberculosis disease. However, treatment of latent tuberculosis infection (LTBI) generally should be delayed until the postpartum period. If a pregnant woman is believed to have been recently infected or is HIV antibody positive, LTBI treatment should not be delayed. Breast-feeding is not a contraindication to LTBI treatment; if a woman being treated with isoniazid is breastfeeding her infant, the infant should be placed on pyridoxine (see page 36).

2. Perinatal exposure. If a pregnant woman has latent tuberculosis infection (LTBI) or tuberculosis disease, her newborn will need special follow up. An infant whose mother is being treated for LTBI should be skin tested at 4 - 6 weeks of age, and if negative, retested at 3 - 4 months and 6 months of age. If the mother is taking isoniazid and breastfeeding her infant, the child should be placed on pyridoxine. The infant would not be placed on isoniazid unless he or she has a positive skin test.

An infant born to a woman being treated for tuberculosis disease should be treated presumptively with isoniazid unless there is evidence of congenital tuberculosis. The child should be checked monthly and then be given a skin test and chest x-ray at 3 - 4 months of age. If the skin test is negative, isoniazid can be stopped and the skin test repeated at 6 months. If the skin test is positive, isoniazid should be continued for a total of 9 months.

An infant born to a woman found to have untreated tuberculosis should be managed the

same as an infant whose mother is being treated for tuberculosis with one additional provision: the mother should be isolated from her infant until treatment of the mother renders her non-infectious.

3. Adults with drug resistant infection.

Unfortunately, no definitive data exist concerning treatment of adults with isoniazid-resistant LTBI. For persons suspected of having isoniazid-resistant, rifampin-sensitive LTBI, a 2 month regimen of rifampin plus pyrazinamide is recommended. If pyrazinamide cannot be tolerated, a 4 month regimen of rifampin can be used. If rifampin cannot be used (due to interaction with antiretroviral drugs), rifabutin can be substituted.

If multidrug-resistant (MDR) LTBI is suspected, either pyrazinamide plus ethambutol or pyrazinamide plus a fluoroquinolone (i.e., levofloxacin or ofloxacin) are recommended if the isolate from the index case is susceptible to these agents. Immunocompromised adults should be treated for 12 months; immunocompetent adults should be observed or treated for at least 6 months. **All persons with MDR-LTBI should be followed for at least 2 years, irrespective of treatment.** A reasonable approach might be to evaluate the patient every 6 to 12 months and, if symptoms warrant, obtain a chest x-ray and sputum specimens for smear and culture.

4. Adults with fibrotic chest lesions. For adults with no evidence of current disease who have a chest x-ray demonstrating old fibrotic lesions thought to represent untreated tuberculosis disease, there are three acceptable regimens for treating LTBI if the infection is unlikely to be drug-resistant:

- 9 months of isoniazid daily or twice weekly,
- 2 months of rifampin *plus* pyrazinamide daily,

- 4 months of rifampin (with or without isoniazid) daily.

These regimens should be given at the standard doses (Table 3). Persons who begin treatment for suspected active pulmonary tuberculosis but are subsequently determined not to have active disease should complete treatment with at least 2 months of a regimen containing rifampin and pyrazinamide unless they have a negative tuberculin skin test or another cause for the chest x-ray abnormalities is established.

Persons with healed primary tuberculosis (e.g., calcified solitary pulmonary nodules, calcified hilar lymph nodes, or apical pleural capping) are not necessarily at higher risk of developing tuberculosis. They should be evaluated for treatment of LTBI based on the criteria on pages 27-28.

Pretreatment evaluation

Prior to starting treatment for latent tuberculosis infection (LTBI), it is critical that the diagnosis of tuberculosis be excluded. If a patient with tuberculosis disease is given a drug regimen for LTBI, drug resistance may develop. Pretreatment evaluation must, at a minimum, include a chest x-ray. Patients whose most recent chest x-ray was taken more than 2 months prior to starting treatment should have a repeat x-ray. If symptoms suggesting either pulmonary or extrapulmonary disease or if abnormalities consistent with pulmonary tuberculosis are present, further diagnostic evaluation is needed. Such evaluation may include comparison of current and previous chest x-rays and bacteriologic examination of sputum. The Tuberculosis Control Program may be able to assist patients in need of a chest x-ray but who lack financial resources. Health-care providers should contact the Program to obtain approval for partial reimbursement before a chest x-ray is taken of a patient who is unable to pay.

Before starting treatment, a patient history should be obtained: key elements include documentation of prior treatment for tuberculosis disease or LTBI, preexisting medical conditions and medications, and risk factors for adverse reactions to drugs used to treat LTBI.

The Tuberculosis Control Program recommends baseline laboratory testing only for patients with specific indications for testing. Patients whose clinical evaluation suggests a liver disorder should have a bilirubin and aspartate aminotransferase (AST; formerly SGOT) or alanine aminotransferase (ALT; formerly SGPT). In addition, baseline testing should be done for patients who are HIV antibody positive, pregnant women and those ≤ 3 months postpartum, persons identified as alcoholics, and adults with whom reliable verbal communication cannot be established (e.g., mentally handicapped patients, some mentally ill patients). If a patient's baseline (pretreatment) AST level is greater than the upper limit of normal for the laboratory at which the testing was done, treatment of LTBI should be delayed or administered cautiously.

Any patient with an indication for baseline liver function testing should also have a baseline complete blood count (CBC) and platelet count if placed on a regimen that includes rifampin or rifabutin.

Assessment of HIV antibody status is indicated for all patients starting treatment for LTBI. Knowledge of a patient's HIV antibody status is important for appropriate medical management, especially since the regimens used for HIV-negative and HIV-positive persons are different. The Tuberculosis Control Program recommends that all patients receiving treatment for LTBI have their HIV antibody status determined if they have any risk factors for HIV infection [MMWR 1989; 38(17):236-8].

TABLE 4. Possible adverse reactions and recommended monitoring for patients being treated for latent tuberculosis infection

Drug	Possible Adverse Reactions	Recommended Monitoring	Comments
Isoniazid	Rash, nausea, vomiting, peripheral neuropathy, elevated liver enzymes, rheumatic syndrome, SLE-like syndrome, mild central nervous system effects. Drug interactions: increases phenytoin and disulfiram levels.	Baseline LFTs indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. Monthly clinical evaluation. Repeat LFTs monthly if patient is pregnant, <3 months postpartum, or at high risk for adverse reaction (alcohol abuse, chronic liver disease, injecting drug user, etc.). Obtain LFTs if signs or symptoms of toxicity are present.	Hepatitis risk increases with age and alcohol consumption. Withhold if transaminase levels exceed three times the upper limits of normal if symptomatic and five times the upper limit of normal if asymptomatic. Pyridoxine indicated for some patients (see text).
Rifampin	Rash, hepatitis, fever, nausea, heartburn, vomiting, ataxia, dizziness, thrombocytopenia, flu-like symptoms, discolored body fluids (urine, sweat, tears). Reduces the level of many drugs including: oral contraceptives, anticoagulants, digitalis, narcotics, beta-blockers, theophylline, and anticonvulsants.	Baseline CBC, platelets, and LFTs indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. If prescribed with pyrazinamide, clinical evaluation at 2, 4, and 8 weeks; otherwise monthly clinical evaluation. Repeat above tests if signs or symptoms of toxicity are present or baseline results are abnormal.	Contraindicated or should be used with caution in HIV-positive persons taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Elevated BUN and serum uric acid has been reported.
Pyrazinamide	Gastrointestinal upset, rash, hepatitis, arthralgia, gout.	Baseline LFTs indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. Clinical evaluation at 2, 4, and 8 weeks. Repeat LFTs if signs or symptoms of toxicity are present or baseline results are abnormal.	Permanently discontinue if signs of hepatocellular damage or hyperuricemia accompanied by acute gouty arthritis develop. Never administer without at least one other anti-tuberculosis drug.
Rifabutin	Rash, hepatitis, fever, arthralgia, thrombocytopenia, uveitis, leukopenia. Discolored body fluids (urine, sweat, tears). Reduces the levels of many drugs including: protease inhibitors, nonnucleoside reverse transcriptase inhibitors, ketoconazole, anticonvulsants, theophylline, dapson, and many others.	Baseline CBC, platelets, and LFTs indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. If prescribed with pyrazinamide, clinical evaluation at 2, 4, and 8 weeks; otherwise monthly. Repeat above tests if signs or symptoms of toxicity are present or baseline results are abnormal.	Contraindicated for HIV-positive persons taking hard-gel saquinavir or delavirdine; caution is advised if administered with soft-gel saquinavir. Decrease dose if taken concurrently with certain protease inhibitors or nonnucleoside reverse transcriptase inhibitors [see MMWR 2000; 49(RR-6):1-51].

Isoniazid is contraindicated for patients with acute liver disease of any cause, prior history of isoniazid-associated hepatitis, severe adverse reactions to isoniazid such as drug fever and arthritis, generalized rash, or central nervous system disturbances (convulsions, toxic psychosis, significant memory loss or personality change), history of medication overdose, or history of severe depression or of suicide attempt or gesture. Patients with a history of medication overdose, severe depression, or suicide attempt or gesture may be treated by directly observed therapy (DOT).

Management during treatment

Treatment of latent tuberculosis infection (LTBI) should be prescribed by the patient's usual medical provider. For patients to whom the cost of private medical care is a barrier to their obtaining appropriate evaluation and treatment of LTBI, the Tuberculosis Control Program may be willing to act as the prescribing health-care provider. Such patients must be adequately evaluated - with a tuberculin skin test, review of symptoms, review of medical history, and chest x-ray - before LTBI treatment is prescribed by the Tuberculosis Control Program.

Before starting treatment, the medical provider should be familiar with drug toxicities and monitoring recommendations (Table 4). These issues are covered in greater detail elsewhere [MMWR 2000; 49 (RR-6):1-51]. Patients taking isoniazid or rifampin alone should be seen on a monthly basis. Those taking rifampin (or rifabutin) plus pyrazinamide should be evaluated at 2, 4, and 8 weeks.

Patients with indications for pretreatment laboratory testing (see above) should have repeat tests done if baseline results were abnormal or if there are symptoms of an adverse reaction (Table 4). Monthly liver function testing should be performed if the patient is taking isoniazid and is either

pregnant, up to 3 months postpartum, or at high risk for adverse reactions (alcohol abuse, chronic liver disease, injecting drug user, etc.). In general, **treatment with isoniazid should be delayed if the AST is three times the upper limit of normal if associated with symptoms or five times the upper limit of normal if the patient is asymptomatic.**

As early in the course of treatment as possible (if not prior to the start of therapy), the most common side-effects of the medicine(s) being taken and the importance of complying with recommended therapy should be discussed with the patient. The patient should be advised to report any changes in health.

Only a 1 month supply of LTBI medicine(s) should be dispensed at a time. Under unusual circumstances (e.g., a patient residing in a remote area with infrequent outside contact), a longer-duration supply may be given to well-motivated patients who appear reliable and who will be able to report any suspected medication-associated side-effects promptly. **Patients should be advised to discontinue medicines temporarily (until a medical evaluation is possible) if they experience possible medication-associated side-effects and cannot immediately contact their health-care provider.**

On a monthly basis, if possible, adult patients or the parent(s) of children taking isoniazid should be asked about the following:

- Unexplained anorexia, nausea or vomiting of 3 or more days duration;
- Fatigue or weakness of 3 or more days duration;
- Signs consistent with liver damage or other toxic effects such as jaundice, persistently dark urine, generalized rash or unexplained fever;
- Persistent paresthesias (manifested as numbness, tingling or other sensory abnormalities) of the hands or feet.

Isoniazid-associated peripheral neuropathy can be treated with oral pyridoxine. Patients taking isoniazid who develop signs or symptoms of hepatitis must be evaluated to determine whether they actually have hepatitis and, if they do, whether the hepatitis is attributable to isoniazid, to one of the hepatitis viruses, or to another agent.

At each encounter with a patient being treated for LTBI, the patient's compliance should be determined. Although there is no absolutely reliable way to do this unless therapy has been directly observed, compliance can be fairly well assessed by questioning the patient and by counting pills remaining since the last refill.

Patients are able to receive isoniazid or other recommended medications for treatment of LTBI free-of-charge through the Tuberculosis Control Program. Physicians and other prescribing health-care professionals can send their prescription (or a copy) to the local public health nurse, Public Health Center, or to the Tuberculosis Control Program. The Tuberculosis Control Program will arrange for the prescription to be filled and can assist in conducting follow-up as described above.

Because patients being treated for LTBI must take their medicine(s) regularly and completely in order to get adequate benefit from treatment, compliance problems should be dealt with as early as possible. For patients who fail to take medicines regularly (e.g., patients who miss 15 days during any 30-day period) discontinuation of treatment should be considered if the patient is at relatively low risk for developing tuberculosis (e.g., a 28-year-old tuberculin reactor without other risk factors). High-risk patients (e.g., household contacts of an infectious tuberculosis case, HIV-positive persons) should be strongly encouraged to take medicine(s) as prescribed, and, if possible, treated using directly observed therapy. Directly observed therapy is an option which the Tuberculosis Control Program can

help arrange. Public health nurses are available to assist other health-care providers develop effective strategies for their patients to comply with treatment recommendations. Contact the Tuberculosis Control Program or the local Public Health Center for assistance.

The incidence of peripheral neuropathy among persons taking isoniazid can be reduced by administration of pyridoxine (vitamin B6). The usual dose of pyridoxine is 50 mg/day for adults or 1-2 mg/kg/day for infants and children. Pyridoxine should be prescribed when isoniazid is administered to:

- persons with conditions in which neuropathy is common (diabetes mellitus, HIV infection, uremia, alcoholism, malnutrition);
- pregnant women and women <3 months postpartum;
- persons with a seizure disorder;
- breastfeeding infants of women who are taking isoniazid.

Completion of treatment

Treatment should be considered complete when the patient has ingested all the drugs prescribed: if doses are missed or there is a gap in treatment, all missed doses should be made up. To be considered adequate, the 9 month daily isoniazid regimen, consisting of 270 doses (30 doses per month x 9 months), should be administered over no more than 12 months. Likewise, to be considered adequate, the 6 month isoniazid regimens should be administered over no more than 9 months. Regimens calling for 2 or 4 months of treatment should be administered over no more than 3 or 6 months, respectively to be considered adequate.

All patients with LTBI (whether treated or not) should be advised to seek medical attention if they develop persistent respiratory symptoms suggestive of tuberculosis. They should then be evaluated for evidence of tuberculosis

disease. Follow-up chest x-rays on asymptomatic patients are not useful and should not be done. No routine follow-up of patients who discontinue LTBI treatment prematurely or who complete a course of treatment is necessary except for one situation: **patients likely to have multidrug resistant LTBI should be followed for at least 2 years, irrespective of treatment.** Medical providers need to be aware that patients who successfully complete an adequate course of treatment for LTBI can still develop tuberculosis disease: treatment reduces, but does not eliminate, the risk of tuberculosis disease.

Updated Recommendations for Use of Rifampin plus Pyrazinamide for Treatment of Latent Tuberculosis Infection (LTBI) – August 31, 2001

These recommendations supercede previous guidelines¹

Between September 2000 and August 2001, 23 cases of serious liver injury were associated with the 2-month course of rifampin-pyrazinamide (RIF-PZA) for LTBI and reported to the U.S. Centers for Disease Control and Prevention (CDC).^{2,3} All of these patients were taking daily RIF-PZA and none were HIV-infected. Six died of liver failure and 17 recovered. After investigation, the CDC and American Thoracic Society presented additional recommendations for the use of RIF-PZA.³

1) Use RIF-PZA with caution, especially with

- persons taking other medications associated with liver injury
- persons with alcoholism, even if alcohol consumption is discontinued
- persons with underlying liver disease
- persons with isoniazid (INH) related liver injury

2) For non-HIV-infected persons with LTBI, 9 months of INH is the gold standard.

- 4 months of daily rifampin is an acceptable alternative to INH.
- 2 months of daily RIF-PZA may be considered if it is unlikely the patient will complete a longer treatment course, does not have risk factors for hepatotoxicity, and can be carefully monitored (Table 1).

3) For HIV-infected persons with LTBI, consider 9

months of daily INH when the patient is likely to complete this longer regimen. RIF-PZA remains an acceptable option for HIV-infected patients; previous clinical trials did not show a high risk of severe hepatitis in this group.

Treatment and monitoring during RIF-PZA therapy

- ✓ Do not give any patient more than a 2-week supply of RIF-PZA at a time.
- ✓ When using the daily regimen, dose PZA at ≤ 20 mg/kg; for the twice-weekly regimen, dose PZA at ≤ 50 mg/kg. (Note: these are lower doses than those used to treat TB disease.)
- ✓ Reassess the patient *in person* at 2, 4, and 6 weeks of treatment, and at 8 weeks to document completion of treatment.
- ✓ Remind the patient at each visit to stop taking RIF-PZA immediately and seek medical care if the following symptoms develop: loss of appetite, malaise, feverishness, nausea or vomiting, jaundice, abdominal pain, or dark urine.
- ✓ Obtain serum AST (SGOT) and bilirubin measurements before starting treatment and at 2, 4, and 6 weeks of treatment. (Note: this recommendation differs from those for laboratory testing for INH and rifampin monotherapy, page 35.)

Table 1. Rifampin plus pyrazinamide for treatment of LTBI

Drugs	Interval	Duration	Medication dose	Monitoring
Rifampin (RIF) plus Pyrazinamide (PZA)	Daily	2 mo.	RIF 10 mg/kg (max. 600 mg) + PZA 15-20 mg/kg (max. 2 gm)	<p>CLINICAL</p> <ul style="list-style-type: none"> • <i>Pretreatment:</i> Ask about history of INH toxicity, use of oral contraceptives and other medications, and liver disease. • <i>During treatment:</i> Wk 2, 4, & 6 check for anorexia, nausea, vomiting, abdominal pain, dark urine, icterus, or fever. Wk 8 check for completion of therapy. <p>LABORATORY</p> <ul style="list-style-type: none"> • Measure AST & bilirubin at 0, 2, 4, & 6 wks for each patient.
	Twice Weekly	2-3 mo.	RIF 10 mg/kg (max. 600 mg) + PZA 50 mg/kg (max. 4 gm) using directly observed therapy (DOT).	

1. American Thoracic Society, CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Resp Crit Care Med* 2000;161:S221-S247.
2. CDC. Fatal and severe hepatitis associated with rifampin and pyrazinamide for the treatment of latent tuberculosis infection—New York and Georgia, 2000. *MMWR* 2000;50:289-91.
3. CDC. Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations—United States, 2001. *MMWR* 2001;50(34):733-5.

Diagnosis of Tuberculosis Disease

Pulmonary tuberculosis should be suspected in persons with a productive, prolonged cough (over 2 weeks duration) which progressively worsens. Other symptoms of tuberculosis include fever, chills, night sweats, easy fatigability, loss of appetite, weight loss and hemoptysis (coughing up blood). The absence of symptoms does not rule out tuberculosis; children, in particular, may have significant mediastinal lymphadenopathy with few or minimal symptoms.

The diagnostic evaluation of persons suspected of having tuberculosis usually includes a Mantoux (PPD) tuberculin skin test, chest x-ray, bacteriologic examination of sputum, and physical examination. Other tests and procedures (i.e., bronchoscopy, biopsy, etc.) may be needed for some patients.

About 15% of tuberculosis cases present with extrapulmonary disease as the major site of involvement. Symptoms of extrapulmonary tuberculosis vary depending upon the site affected, but tuberculosis should be considered in the differential diagnosis of ill persons who are at high risk for tuberculosis [e.g., those with a recent history of exposure, tuberculin skin test converters, immigrants from a country with a high prevalence of tuberculosis, immunosuppressed patients, the elderly, minorities (including Asians and Alaska Natives), the homeless, and other persons from lower socioeconomic groups, etc.].

Indications for collection of sputum specimens

In general, sputum specimens for smear and culture should be obtained to evaluate patients for tuberculosis disease. The following five situations are probably the most common indications for sputum collection:

- The patient is a tuberculin reactor (or converter) and has persistent respiratory symptoms consistent with pulmonary tuberculosis.
- The patient has (a) an abnormal chest x-ray (e.g., an infiltrate, especially if located in the upper lobes); **and** (b) is either a tuberculin reactor or has persistent respiratory symptoms consistent with tuberculosis.
- The patient is (a) a close contact (e.g., household member) of a person with potentially infectious tuberculosis; **and** (b) has persistent respiratory symptoms consistent with tuberculosis. Such a person should also have a Mantoux skin test and a chest x-ray (if an x-ray facility is available or easily accessible).
- The patient has extrapulmonary tuberculosis. Many patients initially diagnosed with extrapulmonary tuberculosis have coexisting pulmonary disease. Three sputum specimens should be obtained from any patient diagnosed with extrapulmonary tuberculosis.
- The patient has pulmonary tuberculosis. Three sputum specimens should be obtained beginning 2 weeks after anti-tuberculosis treatment is started and repeated monthly until all cultures from a single monthly collection are negative. In addition, a series of three sputum specimens should be collected from patients 1 or 2 weeks after completing anti-tuberculosis treatment (irrespective of initial sputum culture results).

Sputum smears or cultures collected for other reasons are exceedingly unlikely to yield positive results and are usually not a good use of laboratory time and materials.

Sputum specimen collection

(see also page 42)

Persons with suspected pulmonary or laryngeal tuberculosis should have at least three sputum specimens examined by smear and culture. If pulmonary or laryngeal tuberculosis is strongly suspected and the initial three sputum smears are negative, additional sputum specimens should be collected. It is desirable that the first specimen be obtained under supervision. For best results, a series of three early morning specimens should be collected on successive (or, at least, separate) days. It is usually indicated to collect sputum specimens from persons with extrapulmonary disease to evaluate their pulmonary status.

To produce good sputum specimens, patients need to know the reason for testing. Patients should be informed that the material brought up from the lungs after a productive cough is sputum. Nasopharyngeal secretions and saliva are not sputum. Coaching each patient individually on how to expectorate can facilitate sputum collection. Patients are seldom successful in providing an adequate specimen if they are not instructed. Coaching is especially necessary in the collection of the first specimen. The amount of support required on subsequent visits will depend on individual patient needs.

For patients unable to raise sputum, aerosol induction using hypertonic saline can stimulate the production of sputum. Patients should be instructed to take several normal breaths of the aerosol mist, inhale deeply, cough with force (while covering their noses and mouths with tissues to avoid contaminating the air), and then expectorate into the specimen container. They should be given time - 15 minutes is usually sufficient - to produce sputum, which in most cases is brought up by a deep cough. Because the

induced sputum is very "watery" and resembles saliva, it should be labeled "induced" to ensure that laboratory staff do not discard it.

The cough induced by the aerosol induction method is often violent and uncontrolled. Therefore, to protect health-care personnel, collection rooms should have some means of air control, such as induction booths equipped with exhaust fans, or portable hoods with HEPA (high efficiency particulate air) filters, ultraviolet light, or a combination of both. Facilities that lack specialized rooms and equipment for specimen collection should minimize exposure to health-care workers by conducting aerosol induction outside.

Gastric aspiration can be used to obtain swallowed sputum. This method is most often used to evaluate young children. Three early morning specimens should be collected. In order to improve the likelihood of recovering *M. tuberculosis* from the stomach, specimens should be obtained immediately after the patient awakens and before they sit or stand. Consequently, for gastric aspirates to be helpful, patients almost always need to be in the hospital overnight.

Bronchoscopy should be done only if the patient cannot produce a sputum specimen and there is reasonable doubt about the diagnosis of tuberculosis. Bronchial washings, brushings, and biopsy specimens may be obtained depending upon the differential diagnostic possibilities and the observed findings. Sputum collected after bronchoscopy may also prove to be diagnostically useful.

Because tuberculosis can occur in almost any anatomical site, a variety of clinical specimens other than sputum may be submitted for examination when extrapulmonary mycobacterial disease is suspected (e.g., urine, cerebrospinal fluid, pleural biopsy and fluid, pus, biopsy specimens, etc.). Tissue specimens

should be placed in saline solution (not in formalin) when they are collected.

Laboratory Examination

1. Smear examination for acid-fast bacilli

Detection of acid-fast bacilli (AFB) on fluorochrome-stained smears examined microscopically may provide the first bacteriologic clue of tuberculosis. Most body fluids or tissues can be examined for the presence of AFB. At the Alaska State Public Health Laboratory, urine and cerebrospinal fluid are not normally examined by AFB smear because they usually contain few organisms; smears of these fluids are almost always AFB-negative, and using some of the specimen for smear examination reduces the volume available for mycobacterial culture.

Results of AFB smears are reported as “no AFB found by fluorochrome stain” or as a qualitative reading from 1+ to 4+. A result of “1+” indicates the presence of a few organisms, whereas a “4+” reading indicates the presence of many organisms. Smears with 10 or fewer AFB are reported as positive and the actual number of AFB seen is reported. AFB smears cannot distinguish M. tuberculosis from other mycobacteria.

2. Mycobacterial culture

Culture examination is essential to confirm the diagnosis of tuberculosis. Because M. tuberculosis grows slowly, several weeks are required for reporting of results. The State Public Health Laboratory sets up parallel cultures for mycobacteria on solid media plates and in liquid media bottles using the BACTEC system. Culture plates are first examined after a 3-week period of incubation. If no growth is noted, a written report is sent to the submitter and the plates are incubated for an additional 3-week period and reexamined. If there is no growth at that time, the plates are discarded; a second written report is not sent. If

colonies morphologically resembling M. tuberculosis are noted after 3 or 6 weeks of incubation, this result is reported by telephone and mail to the facility or person who submitted the specimen and to the Tuberculosis Control Program.

BACTEC is a semi-automated radiometric liquid culture system to detect the growth of mycobacteria more quickly than is possible with conventional solid media. BACTEC cultures may become positive as soon as 1 - 2 weeks after inoculation, depending on the number of viable organisms in the inoculum. Cultures are examined bi-weekly for the first 2 weeks and then weekly for the next 4 weeks. Positive results are reported by telephone and mailed to the submitter and the Tuberculosis Control Program.

Confirmation that an organism detected in either solid media or BACTEC is M. tuberculosis requires testing with a DNA probe. The DNA probe results are reported along with the results of antibiotic susceptibility tests.

3. Antibiotic susceptibility testing

Studies of drug susceptibility on initial isolates are essential for all patients.

Physicians who send specimens to commercial laboratories must make certain that antibiotic susceptibility testing is specifically requested. In the Alaska State Public Health Laboratory, antibiotic susceptibility testing is routinely conducted on all initial isolates of M. tuberculosis; the organisms are tested for sensitivity to isoniazid, rifampin, ethambutol, pyrazinamide, and streptomycin. Susceptibility testing is not done routinely on later isolates of M. tuberculosis from persons whose initial culture(s) yielded M. tuberculosis. Antibiotic susceptibility testing should be requested on the most recent isolate from any patient who continues to have positive cultures 3 months after starting therapy, since this may indicate acquired antibiotic resistance.

4. State Public Health Laboratory instructions

Submit sputum, urine, gastric contents, other body fluids, and tissue specimens in postage-paid mailers provided by the State Public Health Laboratory. The choice of appropriate specimens will depend on the patient's signs and symptoms. Be sure that the screw caps of the plastic centrifuge tubes are tightly closed and that double-walled mailing containers are used.

Mailers designated for tuberculosis testing are only for specimens being tested for tuberculosis - they are not to be used for any other types of specimens or tests. The following instructions are for specimens being submitted to the State Public Health Laboratory for tuberculosis testing:

- (a) The patient's name must be written on the specimen collection tube.
- (b) Fill out the gold (or orange) test request slip in full (see page 109).
- (c) Wrap the specimen collection tube in absorbent material such as a paper towel.
- (d) Place the wrapped specimen collection tube into the metal container, make sure the top is screwed on tightly.
- (e) Wrap the gold (or orange) test request slip around the metal container and place both into the cardboard mailer.
- (f) Generally, specimens should be mailed as soon as possible since delay may lead to bacterial overgrowth; waiting 2 or 3 days is usually acceptable. Refrigerate (do not freeze) until mailed.

(g) Submit specimens to:

State Public Health Laboratory,
P.O. Box 196093
Anchorage, AK 99519-6093

Sputum:

- (a) Instruct the patient to rinse his mouth with

water before collecting sputum specimens. Use sterile 50 mL screw-capped centrifuge tubes available from the State Public Health Laboratory, Anchorage.

- (b) Obtain a series of three early morning specimens collected on consecutive days, before the patient has eaten or taken medicines. A volume of 5 - 10 mL for each specimen is ideal. Smaller volume specimens will be processed by the laboratory if it appears to be sputum, not saliva. Indicate if the specimen was induced.

- (c) Aerosol-induced sputum is usually superior to gastric lavage for recovery of mycobacteria. Do not use propylene glycol as nebulizer. Instead, use aerosolized sterile hypertonic sodium chloride solution.

- (d) Keep specimens refrigerated until mailing. Do not allow to freeze.

Urine:

- (a) Genitals should be washed before the specimen is collected.

- (b) Collect a series of single, first-of-the-morning midstream specimens on 3 successive days. For each urine specimen, at least half of the 50 mL specimen container should be filled. Multiple specimens of this kind are superior to a 24-hour pooled specimen.

- (c) Use 50 mL screw-capped centrifuge tubes. Keep specimens refrigerated; do not freeze. Do not use collection bottles containing preservatives.

Cerebrospinal fluid:

Submit in sterile leakproof containers. No preservative is needed. Keep specimen refrigerated.

Gastric lavage:

Optimally, gastric washings should be collected in sterile containers and processed within 4 hours after collection. Since gastric

acid can kill mycobacteria, an effort should be made to neutralize the pH of the specimen. This can be done in the hospital laboratory by adding 1.5 mL of 40% anhydrous disodium phosphate to every 35 - 50 mL of gastric lavage fluid. Alternatively, the specimen can be diluted with sterile saline solution. Keep the specimen refrigerated until mailing.

Other body fluids, exudates, blood, and tissues:

(a) If necessary, add sterile anticoagulant. Deliver tissue in sterile saline if delay is unavoidable. Do not send preserved or fixed tissue. Blood should always be collected in a tube with anticoagulant.

(b) For blood, collect 10 mL aseptically and submit in an isolator tube.

(c) For stool, submit 5 mL of solid or liquid stool. BACTEC cultures are not done.

Radiographic examinations

A posterior-anterior view of the chest is the standard radiograph needed for detection and description of chest abnormalities. In some cases, other views (e.g., lateral or lordotic) may be necessary. Pulmonary abnormalities are usually found in the apical and posterior segments of the upper lobes or in the superior segments of the lower lobe of patients with tuberculosis. However, lesions may appear anywhere in the lungs and vary in size, shape, and density. Abnormalities on chest radiographs can be suggestive of, but are not diagnostic for, tuberculosis.

The Tuberculosis Control Program provides, with prior approval by its staff, free interpretation of chest x-rays of patients being evaluated for tuberculosis. This service is not intended to be merely a source of free chest x-ray interpretations. "Routine chest x-rays" - for example, chest x-rays of asymptomatic persons who have completed treatment for latent tuberculosis infection, or follow-up chest x-rays

of untreated, asymptomatic tuberculin reactors - are not indicated and will not be accepted for interpretation. In addition, the submitter must provide all pertinent personal data (name, date of birth, place of residence, gender, race, etc.) and clinical information (symptoms/signs, PPD skin test readings, tuberculosis risk factors, relevant past medical history), preferably on a "Tuberculosis Questionnaire/Request for Chest X-ray Interpretation" (pages 100-101), or the film(s) will be returned to the submitter without an interpretation. Routine screening chest x-rays of inmates of correctional facilities and of residents of long-term care facilities should not be sent to the Tuberculosis Control Program for interpretation.

The Tuberculosis Control Program also provides limited reimbursement, if necessary, for chest x-rays of patients who are being evaluated for tuberculosis and who cannot afford such chest x-rays. Reimbursement covers both the x-ray and its interpretation.

Authorization for payment must be approved in advance by Tuberculosis Control Program personnel. The Program does not pay for routine employment chest x-rays and will not reimburse if the patient has health insurance coverage which will pay for the chest x-ray. An authorization number will be provided by the Tuberculosis Control Program when payment is pre-approved. This number must be written on the bill submitted to the program for payment.

Emerging diagnostic tools

Because no method has been found to significantly increase the growth rate of M. tuberculosis *in vitro*, investigators have worked to develop techniques to provide diagnostic information to clinicians faster than is possible with the 3 to 6 weeks necessary for conventional mycobacterial cultures. The development of radiometric culture methods, such as BACTEC, represents a major reduction

in time required before a culture becomes positive. Several other laboratory techniques are in various stages of development; each will be briefly described.

Polymerase chain reaction (PCR) assays. PCR is a method of enzymatic amplification of specific nucleic acid sequences followed by colorimetric detection to determine if the target sequence was present in the initial clinical sample. PCR technology cannot distinguish between viable and dead M. tuberculosis. Because PCR results are available within hours, it is an attractive adjunct to traditional techniques. However, problems with specificity (a high rate of false positives), limit testing to sputum specimens that are AFB smear-positive and are obtained from a patient who has not yet been diagnosed with tuberculosis. An FDA licensed PCR assay, the Amplicor Mycobacterium Tuberculosis Test (manufactured by Roche Diagnostics Systems, Inc.) **is approved only for AFB smear-positive respiratory specimens.** Some laboratories offer “home brewed” PCR assays; these are neither FDA licensed nor recommended by the Tuberculosis Control Program. CDC has published suggestions for using and interpreting PCR tests (MMWR 2000;49:593-4).

Transcriptase-mediated amplification (TMA). The FDA approved a test kit utilizing TMA technology in September 1999. TMA uses transcriptase to enlarge a minuscule quantity of genetic material into a quantity that can be detected by probe. The “Amplified Mycobacterium tuberculosis Direct Test” (or MTD) was developed by Gen-Probe, Inc. The MTD test was licensed for both AFB smear-positive and smear-negative sputum specimens. Although results are available in hours, **testing does not replace AFB smears or mycobacterial cultures, and negative results do not exclude the possibility of pulmonary tuberculosis.** CDC has published suggestions

for using and interpreting TMA tests (MMWR 2000;49:593-4).

High-performance liquid chromatography (HPLC). HPLC is a method used for rapidly identifying M. tuberculosis as well as non-tuberculous mycobacteria species after a solid media culture is found to have growth. Briefly, treated samples of mycobacterial cell wall components are separated chromatographically. The chromatographic pattern is used to identify the mycobacterial species; M. tuberculosis and M. bovis produce essentially the same pattern and thus cannot be distinguished by HPLC. This method is becoming common in large volume mycobacteriology laboratories.

Serologic diagnosis. Serodiagnosis of tuberculosis has been studied for many years with generally disappointing results. Researchers hope that by identifying specific antibodies elicited in response to M. tuberculosis infection, a reliable, simple, and convenient test for tuberculosis infection can be developed. To date, serologic assays do not have satisfactory sensitivity or specificity and such tests have no clinical utility outside the research setting.

A number of other promising technologies are being studied which are intended to provide useful diagnostic information more quickly than is possible using standard culture techniques. Some of these include: immunomagnetic microspheres, tuberculostearic acid, branched DNA signal amplification, reporter mycobacteriophage, Q-beta signal amplification, strand displacement amplification, and ligase chain reaction.

Tuberculosis surveillance case definition

The Tuberculosis Control Program counts a person as a case of tuberculosis if one of the following two criteria, defined by the U.S.

Centers for Disease Control and Prevention (CDC), are met:

1. The case is laboratory confirmed by:
 - a. Isolation of M. tuberculosis from a clinical specimen, or
 - b. Demonstration of M. tuberculosis from a clinical specimen by DNA probe or mycolic acid pattern on high-pressure liquid chromatography, or
 - c. Demonstration of acid-fast bacilli in a clinical specimen when a culture has not been or cannot be obtained.
2. The case is not laboratory confirmed, but all of the following conditions are met:
 - a. The person must have (or have had) a significant reaction to a Mantoux skin test; and
 - b. There must be signs or symptoms compatible with tuberculosis, such as clinical evidence of current disease or an abnormal, unstable (worsening or improving) x-ray; and
 - c. The diagnostic evaluation has been completed and no further diagnostic evaluation is planned; and
 - d. A decision has been made to treat the person with two or more anti-tuberculosis antibiotics.

Persons meeting this case definition are counted, for statistical purposes, as cases of tuberculosis. Failure to meet this case definition does not exclude a clinical diagnosis of tuberculosis. Such patients may be given a presumptive diagnosis of tuberculosis and treated with a full course of anti-tuberculosis therapy by their physicians, but they will not be counted by the Tuberculosis Control Program as cases of tuberculosis unless they meet the above criteria.

Restriction of activities and uncooperative patients

Persons who are suspected to have pulmonary tuberculosis should not ordinarily be allowed to travel by air until either their diagnostic evaluation suggests there is a low risk of transmission or arrangements have been made to reduce the risk of transmission. Specifically, a series of three sputum specimens should be collected from patients who are not in need of immediate transfer. These patients should not fly until they have had three sputum specimen smears which are negative for acid-fast bacilli (AFB). **If an acutely ill patient (either AFB smear positive or untested) who is suspected to have tuberculosis must travel, arrangements should be made with the Tuberculosis Control Program** so that the risk of transmission can be reduced. If a person who should not travel indicates they are unwilling to remain in the community where they are located, the Tuberculosis Control Program should be notified so that commercial air carriers can be informed in order to deny boarding to the person. Although tuberculosis infection has been transmitted on aircraft, it appears that the risk is greatest on flights over 8 hours duration (MMWR 1995; 44:137-140).

Occasionally, a person is encountered who either cannot or chooses not to cooperate with a diagnostic evaluation for tuberculosis. Because such a person represents a potential public health threat (since they could transmit tuberculosis infection to others), health-care providers who have such a patient should inform the Tuberculosis Control Program of the situation. When necessary, the Tuberculosis Control Program will issue an order requiring such a person to submit to a medical examination to detect tuberculosis (Alaska Statute 18.15.135).

Treatment of Tuberculosis Disease

A person with signs or symptoms of tuberculosis should be clinically evaluated. Consultation is available to health-care providers from the Tuberculosis Control Program. All persons suspected or confirmed to have tuberculosis disease must be reported to the Section of Epidemiology's Tuberculosis Control Program (Alaska Administrative Code 7 AAC 27.005). If anti-tuberculosis treatment is thought to be necessary, it should be prescribed by the patient's health-care provider. The Tuberculosis Control Program does not directly evaluate patients with suspected tuberculosis or act as their primary health-care provider. Details of medication doses and schedules can be found in the section titled "Antibiotics Used to Treat Tuberculosis" (pages 59-68). Hospitalized patients should have a comprehensive discharge plan in place prior to leaving the hospital (Appendix 2).

Drug regimens

For all patients with suspected or confirmed tuberculosis, anti-tuberculosis antibiotic therapy is prescribed by their physician or other health-care provider with authority to issue prescriptions. Tuberculosis Control Program personnel will consult with health-care providers about appropriate treatment of tuberculosis disease but do not prescribe treatment.

The three most commonly prescribed regimens, which have relapse rates of less than 5% for patients with fully sensitive isolates are the following (Table 5):

1. Isoniazid, rifampin, and pyrazinamide daily for 8 weeks followed by 16 weeks of isoniazid and rifampin. Daily ethambutol is used initially and continued until susceptibility to isoniazid and rifampin is demonstrated; or

2. Isoniazid, rifampin, pyrazinamide, and ethambutol daily for 2 weeks followed by bi-weekly administration of the same drugs for 6 weeks and then 16 weeks of bi-weekly isoniazid and rifampin; or

3. Isoniazid, rifampin, pyrazinamide, and ethambutol thrice-weekly for 6 months.

The Tuberculosis Control Program strongly recommends that all patients be started on four anti-tuberculosis drugs. Some regimens, not described above, assume that drug-resistance is not present and therefore omit ethambutol. Regimens which include four initial drugs are important in Alaska for two major reasons. First, single and multidrug-resistant *M. tuberculosis* strains are present in Alaska. Of 294 isolates during 1995 to 1999 for which antibiotic susceptibility information was known, 12 or 4% were resistant to one or more drugs. If a tuberculosis patient with an isolate having preexisting isoniazid resistance is treated with a two or three drug regimen, the isolate is likely to develop resistance to rifampin. Multidrug-resistant tuberculosis - which is considerably more difficult to treat and much less likely to be curable - could then be transmitted in the community. Second, sputum conversion, even among patients with fully susceptible organisms, can be accomplished more quickly with a four drug regimen than with a three drug regimen (Ann Intern Med 1990; 112:397-406). More rapid sputum conversion has a potential public health benefit since the patient is rendered noninfectious sooner and a personal benefit to the patient since he or she may be able to resume customary activities sooner.

All patients being treated for pulmonary tuberculosis should receive their medicines as directly observed therapy (DOT).

Furthermore, any regimen administered on a bi-weekly or thrice-weekly basis must be given

TABLE 5. Options for the treatment of uncomplicated tuberculosis¹ in children² and adults

		Dosage (maximum dose) ³		
		Adult	Child ²	
Treatment Option 1	Daily for 8 weeks	isoniazid (INH)	5 (300)	10-20 (300)
		rifampin (RIF)	10 (600)	10-20 (600)
		pyrazinamide (PZA)	15-30 (2 gm)	15-30 (2 g)
		ethambutol (EMB) ⁴	15-25 --	15-25 (2.5 g)
	followed by 16 weeks of <i>either</i>			
	daily	INH	5 (300)	10-20 (300)
		RIF	10 (600)	10-20 (600)
	<i>or</i>			
	2-3 times/week	INH	15 (900)	20-40 (900)
		RIF	10 (600)	10-20 (600)
Treatment Option 2	Daily for 2 weeks	INH	5 (300)	10-20 (300)
		RIF	10 (600)	10-20 (600)
		PZA	15-30 (2 g)	15-30 (2 g)
		EMB ⁴	15-25 --	15-25 (2.5 g)
	followed by 6 weeks of twice weekly	INH	15 (900)	20-40 (900)
		RIF	10 (600)	10-20 (600)
		PZA	50-70 (4 g)	50-70 (4 g)
		EMB ⁴	50 --	50 --
	followed by 16 weeks of twice weekly	INH	15 (900)	20-40 (900)
		RIF	10 (600)	10-20 (600)
Treatment Option 3	Three times weekly for 6 months	INH	15 (900)	20-40 (900)
		RIF	10 (600)	10-20 (600)
		PZA	50-70 (3 g)	50-70 (3 g)
		EMB ⁴	25-30 --	25-30 --

Notes:

1. Consult an expert if a patient remains symptomatic or smear or culture positive after 3 months of treatment. In Alaska, directly observed therapy (DOT) is the standard of care for all patients being treated for pulmonary tuberculosis. Patients on an intermittent regimen must be treated by DOT.
2. Children ≤12 years of age.
3. All doses expressed in mg/kg (maximum doses in mg, except where indicated).
4. Ethambutol should not be discontinued until susceptibility to isoniazid and rifampin have been demonstrated. Except for children being treated daily, maximum doses for ethambutol have not been established. Infants and children ≤6 years of age should be treated with streptomycin rather than ethambutol. Pediatric streptomycin dosing is 20-40 mg/kg (maximum 1.0 g) daily or 25-30 mg/kg (maximum 1.5 g) if given two or three times a week. The total cumulative dose of streptomycin should not exceed 120 g.

as DOT. DOT requires that a health-care provider or other designated person observe the patient ingest anti-tuberculosis medications. The use of DOT has repeatedly been shown to lead to dramatically improved rates of adherence to prescribed anti-tuberculosis treatment [MMWR 1993; 42(RR-7):6-7]. The Tuberculosis Control Program and local public health nurses will help establish DOT programs.

A single drug should never be added to a failing regimen. This common mistake has devastating consequences since resistance is likely to develop to each drug added singly in succession. The result, multidrug-resistant tuberculosis, is much more difficult to treat and is often incurable and fatal. At least two drugs must be used in all phases of treatment of active tuberculosis in order to prevent development of antibiotic resistance.

Continuous administration of drugs, without interruption of more than 14 days, is important to prevent relapse or antibiotic resistance. Drugs must be administered for the prescribed length of time and, to assure that the treatment is adequate, may need to be adjusted if the patient's weight changes. Optimally, to increase absorption, all drugs should be administered on an empty stomach.

Drug resistant tuberculosis

The three previously described regimens may need to be modified, or completely revised, if drug-resistance is found. If isoniazid resistance alone is present, the patient can be treated with rifampin and ethambutol for 12 months. If rifampin resistance alone is present, the patient can be treated with isoniazid and ethambutol for 12 months. If a patient's isolate is resistant to both isoniazid and rifampin, or if the patient cannot be given ethambutol and the isolate is resistant to either isoniazid or rifampin, then a regimen should be developed with the assistance of a tuberculosis specialist. Patients

with suspected multidrug-resistant (MDR) tuberculosis may need to begin with five-drug or six-drug regimens, including at least three drugs to which the strain may be susceptible. Consultation with a tuberculosis specialist will be needed.

Pregnancy and tuberculosis

Untreated tuberculosis represents a far greater hazard to a pregnant woman and her fetus than does treatment of the disease. The initial treatment regimen should consist of isoniazid, rifampin, and ethambutol. These three drugs cross the placenta but are not known to have teratogenic effects. Treatment is for a minimum of 9 months (since pyrazinamide is not included in the initial regimen). Although the routine use of pyrazinamide during pregnancy is precluded by inadequate teratogenicity data, it has been used by some clinicians for many years without apparent adverse effects (Lancet 1995; 346:199). Streptomycin is contraindicated in pregnancy because of its documented ototoxicity in the fetus; kanamycin and capreomycin presumably share this toxic potential. Little information about the risks of cycloserine and ethionamide is available; they should be avoided if possible. Pyridoxine is recommended for pregnant women taking isoniazid. If treatment (with isoniazid) continues into the post-partum period and the patient breastfeeds her infant, the newborn should be placed on pyridoxine (1-2 mg/kg/day).

Extrapulmonary tuberculosis

Regimens for extrapulmonary disease are the same as those recommended for pulmonary tuberculosis. Because less information is available, it is recommended that the duration of treatment be increased to 9 - 12 months for disseminated disease, bone or joint tuberculosis, tuberculous lymphadenitis, or tuberculous meningitis. Adjunctive treatment,

such as surgery or use of corticosteroids, may be beneficial for some cases of extrapulmonary tuberculosis. Corticosteroids have been shown to be beneficial for preventing cardiac constriction from tuberculosis pericarditis and decreasing neurologic sequelae from tuberculosis meningitis, especially if administered early during the course of disease.

Treatment of children

Infants and children with tuberculosis are treated with the same regimens as adults; dosages vary for some drugs (see page 48). Ethambutol is not generally used for children ≤ 6 years of age because their visual acuity cannot be reliably assessed; streptomycin is an alternative. However, because young children with normal renal function rarely experience visual complications from ethambutol, ethambutol may be used when streptomycin is not acceptable.

Pretreatment evaluation and activities

The following pretreatment testing is recommended for persons with tuberculosis disease > 12 years of age:

- Complete blood count (CBC).
- Platelet count (or estimate).
- Serum creatinine and blood urea nitrogen (BUN).
- Hepatic enzyme(s).
- Serum uric acid (if pyrazinamide will be part of therapy).
- Assessment of visual acuity and color perception (if ethambutol will be part of a patient's regimen).
- HIV antibody (if not already known).

The above baseline tests (except visual acuity

and color perception) are not necessary for persons ≤ 12 years of age.

HIV antibody testing should be provided to all patients with tuberculosis disease whose HIV antibody status is not already known. If a patient is HIV positive, anti-tuberculosis therapy should continue for a minimum of 6 months and for at least 4 months after documented culture conversion. Because some of the options for treating tuberculosis in patients with HIV infection are relatively complex, such patients should be treated by a physician experienced in managing tuberculosis and HIV co-infection.

The Tuberculosis Control Program provides anti-tuberculosis medicines free-of-charge to patients with tuberculosis disease (or with latent tuberculosis infection). In order for the Tuberculosis Control Program to dispense these medicines, the health-care provider should send their written prescription to either the local Public Health Center or to the Tuberculosis Control Program. In either case, public health personnel will work with the patient and health-care provider to establish the most appropriate treatment program for the patient.

In most cases no more than a 3-month supply of medicines should be prescribed for a patient at any one time. Medicines will be sent to the public health nurse (or primary care provider), who in turn will give them to a directly observed therapy (DOT) provider or, if DOT is being provided by the nurse, to the patient at a clinic or home visit.

Before beginning anti-tuberculosis treatment, patient education should include: (1) discussion of tuberculosis, its pathogenesis, and its transmission; (2) discussion of the patient's anti-tuberculosis medicines, their side-effects, and what to do if side-effects appear; and (3) discussion of the effectiveness of the medicines and the importance of

compliance with recommended therapy.

All patients being treated for pulmonary tuberculosis should be placed on DOT. The Tuberculosis Control Program will work with the patient's health-care provider and public health nursing to establish the most appropriate DOT program for each new tuberculosis patient. Self-administered medication is seldom, if ever, appropriate. Numerous studies have demonstrated that patient compliance in taking tuberculosis medications is poor, and that health-care providers overestimate patient compliance and cannot reliably predict noncompliance.

The Tuberculosis Control Program works with public health nurses to arrange for DOT. This can include setting-up temporary DOT for patients traveling within Alaska or out of state. Persons suspected or known to have drug resistant tuberculosis or who are on a bi-weekly or thrice-weekly regimens **must** be treated on DOT. The rare patient who self-administers medication should never be given more than a 1-month supply of medicines at a time. Such patients need to be followed very carefully for possible poor compliance. **No parent or guardian should be put in the position of providing DOT for a child with tuberculosis.** Likewise, family members should not be asked to be a DOT provider. Only in very unusual circumstances (e.g., a patient who is leaving for a 2-month trip out of state) should more than a 1-month supply of drugs be given.

Restriction of activities

Patients with pulmonary (or laryngeal) tuberculosis should be considered infectious during **at least** the first 2 weeks of treatment. During this time, they should not go to work or travel by public transit (air, rail, ferry, or bus). Because children with tuberculosis are much less likely than adults to be infectious, they can remain in school unless they either have a cough or their medical evaluation suggests

they are infectious.

Any patient who initially has one or more sputum specimens which are AFB smear or culture positive should not return to school or work until **all three** of the following conditions are met:

- The patient has completed a minimum of 14 days of adequate treatment.
- The patient has demonstrated a favorable clinical response to treatment. This could include a reduction in cough or resolution of fever.
- The patient has had three consecutive negative sputum AFB smears collected on different days.

It is possible that some patients can resume some or all of their usual activities sooner if they are unlikely to expose others to tuberculosis infection. For example, it might be reasonable for a person who works alone on a small fishing boat to return to work while still having AFB positive smears as soon as there has been an adequate response to treatment. Decisions regarding a patient's activities should be made on a case-by-case basis with consultation from the Tuberculosis Control Program.

An occasional patient with tuberculosis may refuse to comply with the prohibition against travel while still infectious. If such a patient is encountered, the Tuberculosis Control Program should be immediately contacted so that actions can be initiated to protect the public health. If necessary, the Tuberculosis Control Program will contact commercial air carriers or other carriers (rail, ferry, etc.) in order to prevent a person with infectious tuberculosis from potentially infecting others.

Monitoring therapy

While being treated for tuberculosis, patients need to be monitored to determine if there is

an adequate response to treatment and if there are any medication side effects. In general, symptoms should begin to improve within several weeks after appropriate anti-tuberculosis therapy is started. Symptomatic improvement should be most rapid in patients with pulmonary tuberculosis; slower improvement would be expected with more indolent forms of tuberculosis such as infection in a bone or joint or central nervous system disease.

All patients (adults and children) should be seen at least monthly while being treated for tuberculosis disease and should be asked about the most common side-effects (see page 60). Routine laboratory monitoring of patients who have normal baseline results is generally not indicated. Patients who report symptoms suggesting drug toxicity should have appropriate laboratory testing performed to confirm or exclude toxic side-effects.

Appropriate therapy should result in rapid conversion of sputum cultures to negative. For patients who are initially sputum AFB smear or culture positive, beginning 2 weeks after therapy is started three sputum specimens for AFB smear and mycobacterial culture should be collected every 4 weeks until all cultures from a single month's collection are negative for mycobacteria. If cultures continue to be positive after the third month of anti-tuberculosis treatment, the patient should be reassessed to determine whether there was failure to comply with recommended therapy or whether the organisms have developed antibiotic resistance. Patients with cavitory disease may take longer to become smear and culture negative.

With pulmonary tuberculosis, the chest x-ray may show improvement within 2-3 months following the initiation of appropriate therapy. For cases which are not culture-confirmed, a follow-up chest x-ray at this time may be useful

to document response to therapy and to give further support for the diagnosis of tuberculosis. Culture-confirmed cases should be followed with serial sputum cultures (as described above) rather than serial chest x-rays.

The nature of follow-up evaluation of patients with extrapulmonary tuberculosis will depend upon the anatomic site(s) involved. Periodic x-ray examinations would be appropriate in cases of pleural disease or skeletal involvement. In cases of meningeal or genitourinary tuberculosis, cultures of cerebrospinal fluid or urine can be used to assess response to therapy. In some instances of extrapulmonary disease, history and physical assessment may be the only appropriate mechanisms for follow-up.

Non-compliant patients

If a patient refuses treatment for pulmonary tuberculosis or is unable or unwilling to cooperate with the prescribed treatment program, the Tuberculosis Control Program should be informed so that appropriate steps can be initiated to confine the patient and protect others in the community. When necessary, the Tuberculosis Control Program will issue orders to protect the public health. Such orders may include authorization to admit and detain a person in a health-care facility or authorization for isolation through detention at the person's place of residence (Alaska Statute 18.15.136). In addition, a court order for the emergency detention of a person in a health-care or other facility will be requested if the person poses a threat to the public health and other measures to protect the public health have not been successful (Alaska Statute 18.15.137).

Completion of therapy

Cultures are more reliable than chest x-rays in demonstrating disease recurrence or ineffectively treated tuberculosis. **Patients with pulmonary tuberculosis (whether or not they were initially culture-positive) should submit three sputum mycobacterial cultures shortly (i.e., 1 or 2 weeks) after completion of therapy.** A chest x-ray at the end of treatment is not necessary but may be useful in the future as a post-therapy baseline. Patients completing therapy should be advised to report signs or symptoms of recurrent tuberculosis.

Indigent patients

Inability to afford medical care and lack of health insurance (or other third-party payment mechanism) should never prevent a patient with suspected or confirmed tuberculosis from receiving medical evaluation and care. The Tuberculosis Control Program will assist indigent patients needing evaluation for tuberculosis (chest x-ray, medical exam, sputum smear or culture) or treatment to receive the necessary services.

Public Health Investigations

Whenever a patient with tuberculosis disease is diagnosed, an epidemiologic investigation should be conducted to identify tuberculosis disease or infection among persons who have been in close contact with the patient. When a tuberculin converter (i.e., a recently infected person) is found, an investigation may be conducted to identify, among that individual's associates, the person with tuberculosis disease who was the source of infection. Contact and associate investigations are a high-yield public health measure for identifying persons with tuberculosis disease and tuberculosis infection.

Definitions

1. A **contact investigation** is the systematic evaluation of persons who have been exposed to a case of tuberculosis for evidence of tuberculosis infection or disease.
2. An **associate investigation** is the systematic evaluation of persons who have been around a person newly infected with M. tuberculosis (i.e., skin test converters, children ≤ 6 years of age) for evidence of tuberculosis infection or disease.

Objectives and priorities

The objectives of contact and associate investigations are: (1) to prevent the development of tuberculosis disease among persons infected with M. tuberculosis by treating latent tuberculosis infection, and (2) to identify persons with tuberculosis disease, so that they can be treated promptly and the transmission of tubercle bacilli can be stopped.

Contact and associate investigations are a public health responsibility and, in Alaska, are primarily conducted by public health personnel. Private and institutional health-care providers who are interested in testing a patient's family members are encouraged to do

so; results will need to be provided to the Tuberculosis Control Program.

Public health investigations to evaluate contacts or associates of the following three types of persons are the highest priority:

- Persons considered to be infectious who have **confirmed** tuberculosis disease. Patients with sputum smear and culture positive disease (or confirmed laryngeal tuberculosis) should be considered potentially infectious and have a contact investigation initiated and completed.
- Persons considered to be infectious who have **suspected** tuberculosis disease. It is appropriate to initiate a contact investigation around a patient with a positive sputum smear and a pending culture if other clinical, laboratory, or epidemiologic evidence suggests that the diagnosis of tuberculosis is likely.
- Children ≤ 6 years of age who have a newly recognized positive tuberculin skin test. An associate investigation of the child's living environment is warranted to protect the child (and siblings, if any) from ongoing exposure to tuberculosis.

Investigations around the following two types of persons should be conducted as resources permit, but never at the expense of the above high priority investigations:

- Persons who have confirmed tuberculosis disease and are unlikely to be infectious. Household contacts of persons with extrapulmonary disease or sputum smear negative disease should usually be investigated since the tuberculosis case may have been infectious earlier in the course of the disease.

- Persons ≥ 7 years of age who are tuberculin skin test converters. Since skin test conversion implies a person was infected at some time during the previous 2 years, it is usually reasonable to evaluate the patient's associates to determine if any of them have unrecognized tuberculosis disease. Associate investigations around persons ≥ 7 years of age with positive tuberculin skin tests who are not skin test converters are generally unproductive and not warranted.

When questions about the nature or extent of a contact or associate investigation arise, it is appropriate to consult with staff of the Tuberculosis Control Program for guidance.

General principals of contact and associate investigations

Cases with far-advanced disease may have been infectious for as long as a year; those with moderately advanced disease may have been infectious for 6 months or longer. Contacts should be identified and examined if they were in close association with the case during the infectious period. The names of contacts or associates living in another area of the state (or outside Alaska) should be provided to the Tuberculosis Control Program for follow-up.

1. Contact investigations: An investigation should be initiated as soon as possible after a case is identified. The investigation may be started before culture results are known if the diagnosis of tuberculosis is highly likely based on the sputum acid-fast bacilli smear results or other clinical information. The first circle of contacts (see page 58) should be identified and have initial Mantoux skin testing completed within 7 days. All skin testing is done using the Mantoux method. Multiple-puncture tests play no role in contact investigations. If any skin test reactors or any tuberculosis cases are identified in the first circle of contacts, then the investigation should be expanded to the second circle of contacts

(consisting of the next most closely exposed group of persons). Each contact should have a decision made regarding treatment within 2 weeks after the Mantoux skin test is read. All contacts with an initially negative skin test must have a follow-up skin test 3 months (or later) after exposure to the infectious case has ended.

2. Associate investigations: The investigation should be initiated as soon as possible after a converter (or reactor ≤ 6 years of age) is identified. The concentric circle approach (see page 58) is used to systematically search for a tuberculosis case (or cases). If the case is not found in the first circle, it may be indicated to widen the investigation. Associates are investigated by means of skin testing, symptom survey, and, when indicated, chest x-ray and sputum examination.

Contact selection

A contact is someone who has been closely associated with a person who has active tuberculosis. Pulmonary tuberculosis and laryngeal tuberculosis are spread through the air by means of droplet nuclei. Therefore, the degree of exposure depends on how much air space has been shared with the patient. Crowding and poor ventilation increase the risk. Household contacts, especially children ≤ 6 years of age and persons with immunosuppression, are at greatest risk of developing tuberculosis infection or disease and should have highest priority in contact follow-up. An important factor that will help indicate how extensive the contact investigation needs to be is the number of household members who have been recently infected. If they are all tuberculin-negative, the patient is probably not highly infectious. If there are tuberculin converters, the patient is likely to be infectious and the contact investigation should be widened beyond the case household.

Exposure to infection ends when the case is removed from the contacts' environment (as when the case is admitted to hospital for anti-tuberculosis therapy) or when the case's sputum cultures become negative. If the tuberculosis patient is at home and has not yet had negative sputum cultures, tuberculin-negative household contacts should be retested every 2 - 3 months, and again 3 months after the patient's sputum cultures become negative. If the contacts' tuberculin tests remain negative 3 months after contact is broken, contacts may be discharged from follow-up and treatment for latent tuberculosis infection discontinued (unless the contact is immunosuppressed; see page 27). Consult with Tuberculosis Control Program staff before discontinuing treatment.

Investigation procedures

Tuberculin test contacts or associates whose most recent skin test was negative or whose tuberculin status is unknown. Only the intermediate-strength (5TU) intradermal Mantoux (PPD) test should be used during an investigation. **Multiple-puncture device skin tests are never used in contact or associate investigations.** Infants can be tested at 4 - 6 weeks and, if negative, retested at 3 - 4 months and 6 months of age. Contacts or associates who have an initial Mantoux skin test with ≥ 5 mm induration should be reported to the Tuberculosis Control Program, and a chest x-ray and symptom survey should be completed to rule out tuberculosis disease. For contacts who have an initial PPD skin test which is negative (< 5 mm), a repeat PPD skin test should be done 3 months after contact is broken.

Two-step skin testing is neither indicated nor appropriate as part of a contact investigation. Two-step testing is designed to identify persons whose sensitivity to tuberculin has waned. But since contacts are persons who

were recently exposed to tuberculosis and therefore may have been recently infected, they have not had time to develop waning sensitivity. In the context of a contact investigation, two-step skin testing cannot distinguish between remotely infected and recently infected persons.

A series of three sputum specimens for acid-fast bacilli smear and mycobacterial culture should be obtained from contacts or associates who are tuberculin reactors or converters with symptoms suggesting tuberculosis. Contacts or associates with signs or symptoms of tuberculosis should be evaluated carefully to rule out disease. If a patient has a positive PPD and signs or symptoms of disease, consult with Tuberculosis Control Program staff.

Contacts or associates who are known to be tuberculin-positive or who have had previous tuberculosis disease have a greater risk of reactivation of latent infection than of becoming reinfected from exposure to an active case. However, contacts and associates with signs or symptoms of tuberculosis disease must be evaluated carefully to rule out disease, and treatment of latent tuberculosis infection (LTBI) should be strongly considered for skin test positive persons who have not had treatment for LTBI or anti-tuberculosis treatment in the past. Furthermore, because previously infected (and treated) persons can be reinfected, it may be reasonable to recommend a course of treatment for LTBI even if a contact has received treatment for LTBI or anti-tuberculosis treatment in the past (N Engl J Med 1993; 328:1137-44). Decisions should be made on a case-by-case basis depending on the specific history, underlying risk factors, and epidemiology of the situation.

The “concentric circle” method

If skin test positive persons are found in the case’s household, the contact investigation should extend to other persons who have shared air space with the active case. The following discussion of a “concentric circle” method of contact investigation may prove helpful in determining the scope of an investigation (Figure 2).

1. First circle of contacts: The first circle of contacts consists of persons who have been in closest and most prolonged contact with the patient, usually the other members of the case’s household. All household members must be evaluated promptly.

If a person with pulmonary tuberculosis has either a cough and a positive sputum smear or a cavitory lesion (or lesions) on chest x-ray, all school classroom contacts, day care contacts, and other persons who have spent significant

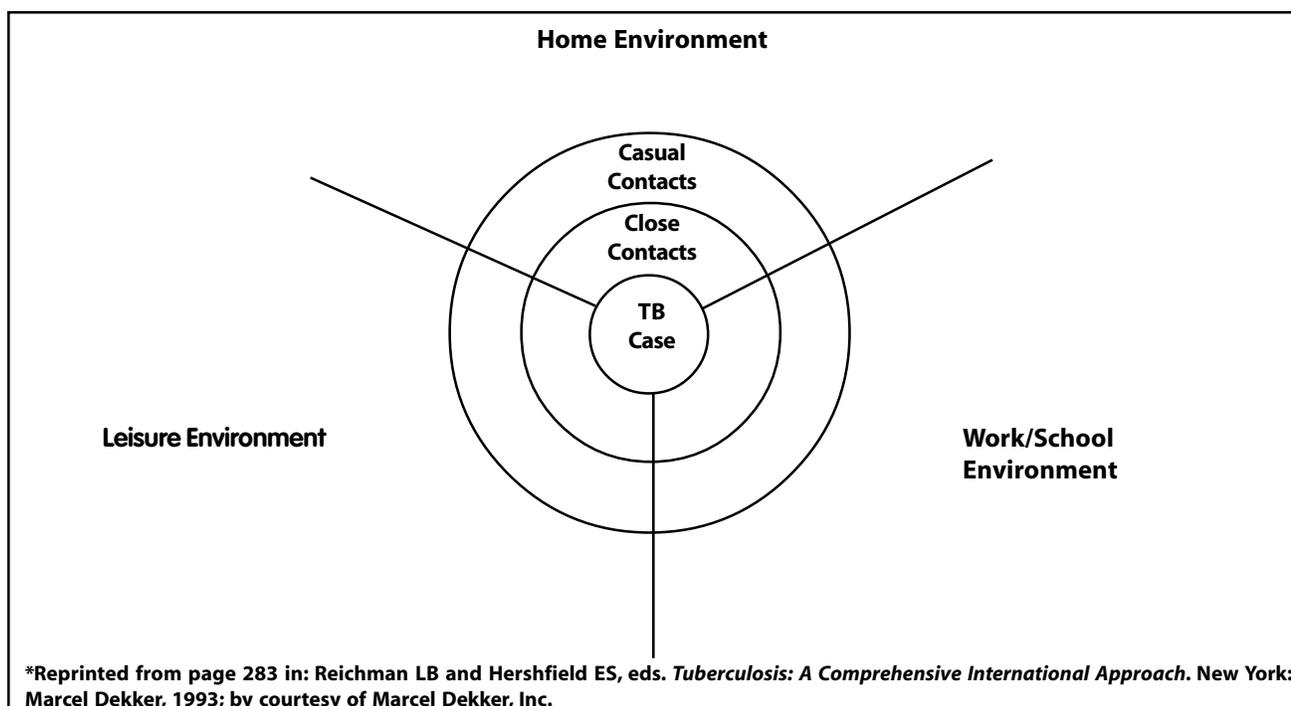
amounts of time with the case in a closed environment should be evaluated. There may be others who, because of intense exposure, should also be tested during this first phase of the investigation.

2. Second circle of contacts: The second circle of contacts consists of persons who have been around a case but have spent less time than persons in the first circle. If any persons in the first circle of contacts are (or seem likely to be) skin test converters, investigation of persons in the second circle will be needed. Persons who may need to be tested includes co-workers, friends, health-care workers, relatives, and others.

Treatment failure

If a tuberculosis patient becomes a treatment failure or relapses, and sputum becomes positive again, a contact investigation should be conducted again. Newly identified contacts must be examined. Exposed, previously uninfected contacts not being treated for LTBI should be reexamined.

FIGURE 2. The concentric circle approach to tuberculosis (TB) contact investigations*



Antibiotics Used to Treat Tuberculosis

A number of effective antibiotics are available for the treatment of patients with tuberculosis. Since single-drug therapy of tuberculosis disease will result in treatment failure and the emergence of drug-resistant organisms, treatment regimens must consist of multiple drugs which have been shown to be effective in combination. **An inappropriate choice of drugs will result in treatment failure, relapse after initial success, and antibiotic resistance.**

The antibiotics used for anti-tuberculosis treatment are classified as bactericidal or bacteriostatic. Each bactericidal drug affects different bacterial populations according to the organisms' metabolic activity and the pH of their environment. Studies have shown streptomycin to be the most effective bactericidal drug for the large, rapidly multiplying extracellular population of tubercle bacilli in cavitary lesions. Pyrazinamide is bactericidal for the intracellular bacilli within macrophages, where the environment is acidic. The action of isoniazid and rifampin is excellent against intracellular bacilli. The slowly and

intermittently multiplying bacilli in closed (non-cavitary), caseous lesions are most susceptible to rifampin. Thus, the combination of isoniazid and rifampin is bactericidal for all three bacterial populations in a tuberculous lesion.

For patients not suspected to have drug resistant tuberculosis, there are three options with relapse rates of less than 5% (Table 5, page 48). It is critical that appropriate doses of each medication be prescribed (Table 6). If sub-therapeutic doses are given, patients are likely to relapse. Patients should be informed of potential side-effects when treatment is started (Table 7). **Second-line anti-tuberculosis drugs (Table 8) should be used only when treatment with first line drugs is not possible** because of drug resistance or toxicity. These drugs should be prescribed by health-care practitioners experienced in their use. **All patients with pulmonary tuberculosis should be treated by directly observed therapy** (see page 51).

TABLE 6. Recommended first-line drugs for the initial treatment of tuberculosis in children¹ and adults

Drug	Daily Dose ²		Twice-Weekly Dose ²		Thrice-Weekly Dose ²	
	Child	Adult	Child	Adult	Child	Adult
Isoniazid	10-20 Max 300 mg	5 Max 300 mg	20-40 Max 900 mg	15 (max) Max 900 mg	20-40 Max 900 mg	15 (max) Max 900 mg
Rifampin	10-20 Max 600 mg	10 Max 600 mg	10-20 Max 600 mg	10 Max 600 mg	10-20 Max 600 mg	10 Max 600 mg
Pyrazinamide	15-30 Max 2 g	15-30 Max 2 g	50-70 Max 4 g	50-70 Max 4 g	50-70 Max 3 g	50-70 Max 3 g
Ethambutol ³	15-25 Max 2.5 g	15-25	50	50	25-30	25-30
Streptomycin ⁴	20-40 Max 1.0 g	15 Max 1.0 g	25-30 Max 1.5 g	25-30 Max 1.5 g	25-30 Max 1.5 g	25-30 Max 1.5 g

Notes: 1. Children ≤ 12 years of age. 2. Dosages are expressed in mg/kg. 3. Generally, ethambutol is not recommended for children whose visual acuity cannot be monitored (≤ 6 years of age). However, ethambutol should be considered for children with organisms resistant to other drugs when susceptibility to ethambutol has been demonstrated or susceptibility is likely. 4. A total cumulative dose of 120 g of streptomycin should not be exceeded unless other therapeutic options are not available.

TABLE 7 . Dosage forms and possible adverse reactions for recommended first-line drugs for the initial treatment of tuberculosis in children and adults

Drug	Dosage Forms	Possible Adverse Reactions
Isoniazid ^{1,2}	Tablets: 100 mg, 300 mg Vials: 1 g	Hepatic enzyme elevation, neuropathy, hepatitis, peripheral neuritis, hypersensitivity
Rifampin ^{1,2}	Capsules: 150 mg, 300 mg Syrup: formulated from capsules, 10 mg/ml	Orange discoloration of secretions and urine, nausea, vomiting, hepatitis, febrile reaction, purpura (rare)
Pyrazinamide ²	Tablets: 500 mg	Hepatotoxicity, hyperuricemia
Ethambutol	Tablets: 100 mg, 400 mg	Optic neuritis (decreased red-green color discrimination, decreased visual acuity), skin rash
Streptomycin	Vials: 1 g, 5 g	Ototoxicity, nephrotoxicity

Notes: 1. Isoniazid (150 mg) and rifampin (300 mg) are available as a combination in Rifamate. 2. Isoniazid (50 mg), rifampin (120 mg), and pyrazinamide (300 mg) are available as a combination in Rifater.

TABLE 8. Second-line anti-tuberculosis drugs¹

Drug	Dosage Forms	Daily Dose in Children and Adults ²	Maximal Daily Dose	Major Adverse Reactions	Recommended Regular Monitoring
Capreomycin	Vials: 1 g	15 mg/kg, IM	1 g	Auditory, vestibular, and renal toxicity	Vestibular function, audiometry, blood urea nitrogen, and creatinine
Kanamycin	Vials: 75 mg, 500 mg, 1 g	15 to 30 mg/kg, PO	1 g	Auditory and renal toxicity, rare vestibular toxicity	Vestibular function, audiometry, blood urea nitrogen, and creatinine
Ethionamide	Tablets: 250 mg	15 to 20 mg/kg, PO	1 g	Gastrointestinal disturbance, hepatotoxicity, hypersensitivity	
Para-aminosalicylic acid (PAS)	Tablets: 500 mg Delayed release granules: 4 g/packet	150 mg/kg, PO	12 g	Gastrointestinal disturbance, hepatotoxicity, hypersensitivity sodium load	Hepatic enzymes
Cycloserine	Capsules: 250 mg	15 to 20 mg/kg, PO	1 g	Psychosis, convulsions, rash	Assessment of mental status
Ciprofloxacin	Tablets: 250 mg, 500 mg	500-750 mg, PO, BID	2 g	Gastrointestinal disturbance, headache, rash, photosensitivity, drowsiness, renal dysfunction. Interacts with coumadin, theophylline, and antacids	Check serum levels
Ofloxacin	Tablets: 200 mg, 300 mg, 400 mg	400-800 mg, PO, BID	1.6 g	As with ciprofloxacin	Check serum levels

Notes: 1. These drugs are more difficult to use than the drugs listed in Table 7. They should only be used when treatment with first-line drugs is not possible (because of drug resistance or toxicity) and they should be given and monitored by health-care providers experienced in their use. 2. Doses based on weight need to be adjusted as weight changes.

Isoniazid

(Trade names: Armazide, Cotinazin, Dituban, Ertuban, Hyzyd, Isozide, Neoteben, Niadrin, Niconyl, Nidaton, Nydrasid, Panazid, Rimifon, Tisin, Tyrid; contained in Rifamate, Rifater.)

1. Action: Bactericidal to both extracellular and intracellular organisms.
2. Dose: Although isoniazid is available as a syrup, its use in this form is discouraged because of unpredictable absorption.

Regimen	Dose (mg/kg)		Maximum (child or adult)
	Child*	Adult	
Daily	10-20	5	300 mg
Bi-weekly	20-40	15	900 mg
Thrice-weekly	20-40	15	900 mg

* Child \leq 12 years of age.

3. Contraindications:
 - a. Previous isoniazid-associated liver injury.
 - b. Acute liver disease of any cause.
 - c. Severe adverse reactions to isoniazid, such as drug fever or arthritis.
 - d. Severe renal dysfunction (relative contraindication).
 - e. History of medication overdose, depression, or suicide gesture or attempt (relative contraindication).
 - f. Early pregnancy (relative contraindication).
4. Drug interactions:
 - a. Alcohol - Associated with higher incidence of isoniazid-related hepatitis.
 - b. Phenytoin (Dilantin) - Isoniazid increases absorption of phenytoin. Serum levels of both drugs rise when they are administered together; therefore, serum phenytoin levels must be closely monitored when treatment with isoniazid is started.
 - c. Aluminum hydroxide (in some antacids) - Decreases absorption of isoniazid.
5. Adverse reactions:
 - a. Isoniazid-associated hepatitis. The risk of isoniazid-associated hepatitis is age-related. A large study of patients taking isoniazid alone for treatment of latent tuberculosis infection found the following rates of hepatitis:

0 cases per 1000 persons under age 20 years;
 3 cases per 1000 persons aged 20-34 years;
 12 cases per 1000 persons aged 35-49 years;
 23 cases per 1000 persons aged 50-64 years;
 8 cases per 1000 persons older than 64 years;

- b. Peripheral neuropathy.
- c. Other peripheral nervous system effects (optic neuritis, muscular twitching).
- d. Central nervous system effects (sedation, seizures, toxic encephalopathy, psychosis, stupor, euphoria, dizziness, memory impairment).
- e. Arthritis.
- f. Gastrointestinal effects: nausea, vomiting, epigastric distress.
- g. Hypersensitivity: drug fever, skin rash, purpura, urticaria, vasculitis.
- h. Lupus-like syndrome (fever, arthralgia, myalgia, abdominal pain).
- i. Hematologic reactions: agranulocytosis, thrombocytopenia, eosinophilia.

6. Overdose: Manifestations of isoniazid overdose include obtundation (which may end in coma and death), intractable major motor seizures, metabolic acidosis (often severe), respiratory distress (frequently with aspiration pneumonia), and hypotension. Signs or symptoms have been noted in adults following ingestion of as little as 3 g. Isoniazid overdose should be suspected in a patient of any age who presents with any of the above signs or symptoms. Isoniazid overdose is a medical emergency and the patient should be evaluated in the nearest hospital emergency room.

7. Recommended medical monitoring: Baseline liver function tests (LFTs) indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. Monthly clinical evaluation. Repeat LFTs monthly if patient is pregnant, <3 months postpartum, or at high risk for adverse reaction (alcohol abuse, chronic liver disease, injecting drug user, etc.). Obtain LFTs if signs or symptoms of toxicity are present. See also "Pretreatment evaluation" and "Management during treatment" (pages 33-36).

Rifampin

(Trade names: Rifadin, Rimactin, Rifagen, Rifaldin, Rifobac, Rifocin; contained in Rifamate, Rifater.)

1. Action: Bactericidal.
2. Dose: The dosage of rifampin is the same for patients treated on the daily, bi-weekly, or thrice-weekly regimen. Different dosages may be used for treatment of latent tuberculosis infection (see page 30).

Adults: 10 mg/kg up to 600 mg

Children:* 10 - 20 mg/kg up to 600 mg

*Children \leq 12 years of age.

Note: Absorption of rifampin may be enhanced if taken on an empty stomach.

3. Contraindications: History of hypersensitivity reaction to any of the rifamycins.
4. Drug interactions: Rifampin induces hepatic microsomal enzymes which increase the rate at which certain other drugs are metabolized and excreted.
 - a. Oral hypoglycemic agents (sulfonylureas, glipizide, glyburide): activity is decreased.
 - b. Oral anticoagulants (coamadin, warfarin sodium): anticoagulant dosage requirement is increased.
 - c. Oral contraceptives and female hormones (ethinyl estradiol, ethynodiol diacetate, levonorgestrel, mestranol, norethindrone, norethynodrel, norgestrel): may decrease effectiveness.
 - d. Cardiac glycosides (digitoxin, digoxin, disopyramide, quinidine): pharmacologic activity is decreased.
 - e. Oral corticosteroids (betamethasone, cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, triamcinolone): activity is decreased.
 - f. Cyclosporine: plasma level is decreased.
 - g. Theophylline: activity is decreased.
 - h. Ethambutol: potential for thrombocytopenia.
 - i. Ketoconazole: blood level is reduced.
 - j. Methadone hydrochloride: may reduce blood concentration to a degree sufficient to cause withdrawal symptoms.
 - k. Incidence of liver disease is increased in persons taking other hepatotoxic drugs.
 - l. Para-aminosalicylic acid (PAS) reduces absorption of rifampin.

5. Adverse reactions:

- a. Liver dysfunction: Jaundice occurs in 0.6% of patients. The risk of liver disease is increased in persons with prior liver disease or also taking isoniazid. Minimal liver enzyme abnormalities are common. In patients taking both isoniazid and rifampin, predominant elevation of serum alkaline phosphatase and bilirubin suggests rifampin toxicity; predominant elevation of transaminases may be due to toxicity from isoniazid, rifampin, or both drugs.
 - b. High-dose intermittent therapy (i.e., poorly compliant patients) or reinstatement of rifampin after a drug-free interval has been associated with severe, rarely fatal side-effects:
 - Autoimmune hemolytic anemia and thrombocytopenia.
 - Respiratory distress: wheezing or dyspnea resembling asthma, shock.
 - Acute renal failure, hepatorenal syndrome.
 - "Flu-like" syndrome: fever, chills, myalgia, arthralgia, vomiting, diarrhea.
 - c. Hypersensitivity: cutaneous flushing, conjunctivitis, urticaria.
 - d. Central nervous system effects: headache, drowsiness, fatigue, inability to concentrate, visual disturbances.
 - e. Gastrointestinal disturbances.
 - f. Discoloration of body fluids: rifampin imparts an orange-pink color to saliva, tears, urine, and sweat and stains soft contact lenses; this effect is innocuous.
6. Overdose: Overdose is characterized by nausea, vomiting, and increasing lethargy. Severe hepatic involvement may follow.
 7. Recommended medical monitoring: Baseline CBC, platelets, and liver function tests (LFTs) indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. If prescribed with pyrazinamide, clinical evaluation at 2, 4, and 8 weeks; otherwise monthly clinical evaluation. Repeat above tests if signs or symptoms of toxicity are present or baseline results are abnormal. See sections titled "Pretreatment evaluation" and "Management during treatment" (pages 33-36).

Pyrazinamide

(Trade names: Aldinamid, Tebrazid, Zinamide; contained in Rifater.)

1. Action: Bactericidal in acid medium (intracellular). Bacteriostatic in alkaline medium (extracellular).
2. Dose: The dosage is the same for children and adults.
Daily: 15 - 30 mg/kg up to 2 g
Bi-weekly: 50 - 70 mg/kg up to 4 g
Thrice-weekly: 50 - 70 mg/kg up to 3 g
3. Contraindications: Abnormal liver function tests (relative contraindication). Because of inadequate teratogenicity data, pyrazinamide is generally not used during pregnancy.
4. Drug interactions: None known.
5. Adverse reactions:
 - a. Hepatitis: Uncommon; occurs in no more than 1 - 2% of persons. Pyrazinamide contributes no additional hepatotoxicity when added to a regimen of isoniazid and rifampin.
 - b. Arthralgias.
 - c. Hyperuricemia: Acute gout occurs in some patients with hyperuricemia due to pyrazinamide. Discontinuation of pyrazinamide should be considered if the patient has gout and the serum uric acid exceeds 15 mg/dL. Arthralgia can be controlled with aspirin, probenecid, or allopurinol. Patients with asymptomatic hyperuricemia can continue taking pyrazinamide.
 - d. Dermatologic effects: Flushing, cutaneous hypersensitivity reactions, photosensitization.
 - e. Gastrointestinal effects: anorexia, nausea, vomiting.
 - f. Sideroblastic anemia (rare, reversible).
6. Overdose: Experience treating overdoses is limited. Abnormal liver function tests may develop. Clinical monitoring and supportive therapy should be employed.
7. Recommended medical monitoring: Baseline liver function tests (LFTs) indicated for HIV positive persons, pregnant and postpartum women, persons with chronic liver disease, and regular alcohol users. Clinical evaluation at 2, 4, and 8 weeks. Repeat LFTs if signs or symptoms of toxicity are present or baseline results are abnormal.

Ethambutol

(Trade names: Myambutol, Etambol, Inagen, Mycobutol, Olbutam.)

1. Action: Bacteriostatic.
2. Dose: The dosage is the same for children and adults.
Daily: 15 - 25 mg/kg (up to 2.5 g for children)
Bi-weekly: 50 mg/kg
Thrice-weekly: 25 - 30 mg/kg
3. Contraindications:
 - a. Known hypersensitivity to ethambutol.
 - b. Patients with known optic neuritis.
 - c. Ethambutol should not be used in patients with impaired vision and in children ≤ 6 years of age unless visual acuity and color discrimination can be reliably assessed. Because young children with normal renal function rarely experience visual complications from ethambutol, ethambutol may be used when streptomycin is not acceptable.
 - d. Impaired renal function.
4. Drug interactions: None known.
5. Adverse reactions:
 - a. Retrobulbar neuritis: Very uncommon at recommended dosages. Effects are slowly reversible if the drug is stopped as soon as they are detected, but can progress to optic atrophy and permanent blindness if continued. Two types of retrobulbar neuritis are possible: (1) axial - causes reduced visual acuity, central scotoma and disturbances of red-green perception; (2) periaxial (less common) - causes peripheral field defects.
 - b. Other adverse reactions include mild hyperuricemia, peripheral neuropathy, and rarely, hepatitis and hypersensitivity.
6. Overdose: Symptoms may include abdominal pain, fever, confusion, nausea, hallucinations, and, if the overdose exceeds 10 g, optic neuropathy. Treatment is symptomatic and supportive. Vitamin B12 has had some success in treating optic neuritis.
7. Recommended medical monitoring: Visual acuity and red-green perception should be tested prior to the start of therapy and monthly thereafter. If there is more than a one-line decrease in visual acuity (on Snellen eye chart) or if there is loss of color discrimination, ethambutol should be discontinued. For closer monitoring, patients may be instructed to read small print in the newspaper every day and to report any change.

Streptomycin

(Trade names: Strycin, Streptolin, Streptaquaine.)

1. Action: Bactericidal in alkaline medium (extracellular). Bacteriostatic in acid medium (intracellular).
2. Dose: A total cumulative dose of more than 120 g should not be given unless other therapeutic options are not available.

Regimen	Dose (mg/kg)		Maximum (adult or child)
	Child*	Adult	
Daily	20-40	15	1.0 g
Bi- or thrice-weekly	25-30	25-30	1.5 g

*Child \leq 12 years of age.

3. Contraindications: Streptomycin is contraindicated in persons who have shown a previous toxic or hypersensitivity reaction to it.
 - a. Avoid use in patients with middle or inner ear disease, because of ototoxicity.
 - b. Avoid use in patients with myasthenia gravis, because streptomycin is a weak neuromuscular blocker.
 - c. Avoid use in pregnant women, because of potential ototoxic effect on the fetus.
 - d. Use with caution in patients with impaired renal function.
 - e. Avoid use in persons with known sensitivity or allergy to sulfites.
4. Drug interactions: The concurrent or sequential use of other neurotoxic or nephrotoxic drugs, such as neomycin, kanamycin, gentamicin, cephaloridine, paromomycin, viomycin, polymixin B, tobramycin, and cyclosporine, should be avoided.
5. Adverse reactions:
 - a. Ototoxicity: Streptomycin has a selective toxic action on the eighth cranial nerve. Vestibular damage (manifested by vertigo, dizziness, nausea) is more common than auditory damage, although both occur. Ototoxicity is more common in infants and in persons over 40 years of age; in the latter group, recovery is slower and often less complete. Ototoxicity is related to both the cumulative dose and peak serum concentrations. Toxicity is more likely if other ototoxic drugs are given concurrently. The dosage should be reduced (or its use avoided altogether) in persons over 60 years of age.
 - b. Renal toxicity: Nephrotoxicity is related both to cumulative dose and to peak serum concentrations; the

risk may be increased in patients with preexisting renal insufficiency or with simultaneous use of other nephrotoxic drugs. The dose should be reduced in elderly patients and in persons with renal impairment. Severe renal damage is rare.

- c. Hypersensitivity: rash or fever are common in patients and occasionally seen in persons handling the drug; anaphylaxis is rare.

- d. Other neurotoxic effects: ataxia, transient giddiness, peripheral neuropathy (especially circumoral numbness).

- e. Neuromuscular blockade.

- f. Rare adverse reactions: aplastic anemia, agranulocytosis, lupoid reactions.

6. Overdose: Overdose may cause renal damage or ototoxicity. The serum streptomycin level should be monitored and baseline serum creatinine and BUN measured. Treatment is generally symptomatic and supportive.

7. Recommended medical monitoring:

- a. Renal: Measure the BUN and creatinine before and periodically during treatment in patients with renal disease or receiving dosages greater than 1 g twice a week.

- b. Vestibular: Periodically do a Romberg test (while patient stands with feet close together and eyes closed, check for swaying of the body or near-falling). Check for history of dizziness or unsteadiness of gait, especially when patient is in the dark or when eyes are closed.

- c. Auditory: Periodically check patient's ability to hear whispered words at 20 feet or the ticking of a watch 1 - 3 inches from the ear. Test each ear separately and, where appropriate, do an audiogram.

Cycloserine

(Trade names: Seromycine, Aristoserina, Closina, Farmiserina, Oxamycin, Tisomyacin.)

1. Action: Bacteriostatic
2. Dose: 15 - 20 mg/kg up to 1.0 g for children or adults.
3. Contraindications:
 - a. Known hypersensitivity to cycloserine.
 - b. Epilepsy.
 - c. Depression, severe anxiety, or psychosis.
 - d. Severe renal insufficiency.
 - e. Excessive use of alcoholic beverages.
4. Drug interactions:
 - a. Alcohol: Increased risk of seizures.
 - b. Ethionamide: Neurotoxic side-effects are potentiated.
 - c. Other anti-tuberculosis drugs (isoniazid, rifampin, ethambutol): Concurrent use may result in vitamin B12 or folic acid deficiency and an increased incidence of central nervous system effects such as dizziness or drowsiness.
5. Adverse reactions: adverse reactions to cycloserine are common and often dose-related.
 - a. Neurologic effects (drowsiness, confusion, dizziness, convulsions, hyperreflexia, dysarthria, vertigo, insomnia, tremor): these effects are usually seen with dosages exceeding 500 mg/day.
 - b. Psychiatric effects: personality change, psychosis, disorientation, memory loss, depression, anxiety.
 - c. Hypersensitivity (allergic skin rash).
 - d. Miscellaneous: elevated serum transaminase (rare), especially in patients with preexisting liver disease; megaloblastic anemia (rare).
6. Overdose: Acute toxicity can occur if more than 1 g is ingested by an adult. Toxic effects include headache, vertigo, confusion, drowsiness, dysarthria, and psychosis. Paresis, convulsions, and coma may occur after a large overdose. Overdose is a medical emergency and should be managed at a hospital.
7. Recommended medical monitoring: Cycloserine levels should be determined periodically for patients with reduced renal function, for persons receiving >500 mg daily, and for those showing signs and symptoms suggestive of toxicity.

Ethionamide

(Trade names: Trecator, Iridocin, Trescatyl, Tubenamide.)

1. Action: Bacteriostatic
2. Dose: 15 - 20 mg/kg up to 1.0 g.
3. Contraindications:
 - a. Preexisting liver disease.
 - b. Severe hypersensitivity.
 - c. Pregnancy.
4. Drug interactions:
 - a. Cycloserine: convulsions; adverse effects may be intensified.
 - b. Other anti-tuberculosis drugs (isoniazid, rifampin, ethambutol): adverse effects may be intensified.
5. Adverse reactions
 - a. Gastrointestinal symptoms: gastric irritation, nausea, metallic taste, vomiting, diarrhea, anorexia, abdominal pain, and excessive salivation. Nausea may be controlled by administering ethionamide at bedtime or administering it with antacids.
 - b. Hypersensitivity reactions: photosensitivity.
 - c. Hepatitis (uncommon).
 - d. CNS effects: giddiness, headache, depression, drowsiness.
 - e. Miscellaneous: alopecia, convulsions, deafness, diplopia, gynecomastia, hypotension, impotence, menstrual irregularity, hypoglycemia, peripheral neuropathy. All are rare.
6. Overdose: Specific information concerning ethionamide overdose is limited. Patients felt to have an ethionamide overdose should have a careful medical evaluation. Treatment is generally symptomatic and supportive.
7. Recommended medical monitoring: No routine monitoring is necessary, but periodic hepatic enzyme testing may be indicated in patients with an increased risk of liver damage.

Capreomycin

(Trade name: Capastat.)

1. Action: Bacteriostatic.
2. Dose: 15 mg/kg up to 1.0 g.
3. Contraindications:
 - a. Renal insufficiency.
 - b. Preexisting auditory impairment.
 - c. Pregnancy.
 - d. Safety in children ≤ 12 years is unknown.
 - e. Known hypersensitivity to capreomycin.
4. Drug interactions:
 - a. Anti-tuberculosis drugs (isoniazid, rifampin, ethambutol, cycloserine): febrile reactions and abnormal liver function tests.
 - b. Aminoglycoside and polypeptide antibiotics (colistin, gentamicin, kanamycin, neomycin, streptomycin, tobramycin, vancomycin, and others): additive ototoxicity and nephrotoxicity.
 - c. Ether: neuromuscular block is enhanced.
 - d. Anticholinesterase agents (neostigmine): neuromuscular block is antagonized.
5. Adverse reactions:
 - a. Nephrotoxicity: Renal injury, with elevation of the BUN above 30 mg/dL or other evidence of decreasing renal function, calls for careful evaluation and reduction of the dosage or stoppage of the drug.
 - b. Ototoxicity (may affect both auditory and vestibular function).
 - c. Hypokalemia.
 - d. Pain and induration at the injection site.
 - e. Hypersensitivity reactions.
 - f. Eosinophilia.
6. Overdose: Oral ingestion is unlikely to result in toxicity since the drug is poorly absorbed. Parenteral overdose may cause damage to auditory and vestibular nerves and neuromuscular blockage or respiratory paralysis. Patients should be managed in a hospital.
7. Recommended medical monitoring:
 - a. Audiometric measurements and assessment of vestibular function prior to initiation of therapy and at regular intervals during treatment.
 - b. Weekly tests of renal function.
 - c. Frequent serum potassium levels.

Para-aminosalicylic acid

1. Action: Bacteriostatic.
2. Dose: 150 mg/kg up to 12 g.
3. Contraindications: Pregnancy.
4. Drug interactions:
 - a. Phenytoin: phenytoin toxicity may develop when phenytoin and para-aminosalicylic acid are taken concurrently.
 - b. Rifampin: interferes with absorption of rifampin.
5. Adverse reactions:
 - a. Gastrointestinal tract irritation: anorexia, nausea, vomiting, diarrhea, steatorrhea, malabsorption. Symptoms are less common in children than in adults. Administration with antacids may reduce symptoms.
 - b. Hypersensitivity reactions (common) may include fever, skin rash, conjunctivitis, headache, arthralgias, lymphadenopathy, jaundice, blood dyscrasias, Loeffler's syndrome, and a mononucleosis-like syndrome.
 - c. Hypothyroidism and goiter (disappear when discontinued).
 - d. Excessive sodium load (when sodium salt is administered) in some patients.
 - e. Acute renal failure (rare).
 - f. Hematologic reactions: hypoprothrombinemia (mild), hemolytic anemia, thrombocytopenia.
6. Overdose: Overdoses have not been reported and specific information on symptoms or treatment is limited. Patients felt to have a para-aminosalicylic acid overdose should have a careful medical evaluation. Treatment is generally symptomatic and supportive.
7. Recommended medical monitoring: Liver enzymes should be measured once a month.

Ciprofloxacin

(Trade name: Cipro.)

1. Action: Weakly bactericidal.
2. Dose: 500 - 750 mg twice daily.
3. Contraindications: This drug should not be administered to pregnant women or children unless the risks to the fetus or child have been carefully considered.
4. Drug interactions:
 - a. Theophylline: prolonged half-life with increased serum levels and potential for toxicity.
 - b. Antacids: antacids containing aluminum, magnesium, or calcium may interfere with absorption of ciprofloxacin.
 - c. Ferrous sulfate: may interfere with absorption of ciprofloxacin.
5. Adverse reactions:
 - a. Gastrointestinal disturbance.
 - b. Dizziness.
 - c. Hypersensitivity.
 - d. Elevated aspartate aminotransferase or alanine aminotransferase.
 - e. Eosinophilia.
 - f. Leukopenia.
 - g. Elevated serum creatinine.
 - h. Photosensitivity.
6. Overdose: The stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed and given supportive treatment, including adequate hydration.
7. Recommended medical monitoring: Serum levels should be monitored.

Ofloxacin/Levofloxacin

(Trade names: Floxin, Levaquin.)

1. Action: Weakly bactericidal.
2. Dose: Ofloxacin 400 - 800 mg twice daily.
Levofloxacin 500 - 750 mg daily.
3. Contraindications: These drugs should not be administered to pregnant women or children unless the risks to the fetus or child have been carefully considered.
4. Drug interactions:
 - a. Theophylline: concurrent administration may result in increased theophylline levels.
 - b. Warfarin: enhanced effects of warfarin and its derivatives are possible.
 - c. Antidiabetic agents: hyperglycemia and hypoglycemia may occur more frequently in patients treated concurrently with an antidiabetic drug (insulin or oral agents).
 - d. Antacids: antacids containing aluminum, magnesium, or calcium interfere with absorption of ofloxacin and levofloxacin.
 - e. Ferrous sulfate: may interfere with absorption of ofloxacin.
5. Adverse reactions:
 - a. Gastrointestinal upset.
 - b. Headache.
 - c. Insomnia.
 - d. Leukopenia, leukocytosis.
 - e. Elevated alkaline phosphatase, aspartate aminotransferase.
 - f. Elevated creatinine, BUN.
 - g. Photosensitivity.
6. Overdose: There are limited data on ofloxacin or levofloxacin overdoses. In the event of an oral overdose, the stomach should be emptied and the patient given supportive treatment.
7. Recommended medical monitoring: Serum levels should be monitored.

Kanamycin

(Trade name: Kantrex.)

1. Action: Bactericidal.
2. Dose: 15 - 30 mg/kg.
3. Contraindications:
 - a. Patients with impaired renal function must be managed carefully.
 - b. Pre-existing auditory or vestibular impairment.
 - c. Pregnancy.
 - d. Known hypersensitivity to kanamycin.
4. Drug interactions: The concurrent use of other agents with nephrotoxic potential should be avoided.
5. Adverse reactions:
 - a. Eosinophilia: Up to 10% of patients develop eosinophilia with or without other signs of allergy such as fever, rash, pruritis, and anaphylaxis.
 - b. Ototoxicity: May affect both auditory and vestibular function.
 - c. Nephrotoxicity.
6. Overdose: Parenteral overdose may cause auditory and vestibular nerve damage, neuromuscular blockade, or respiratory paralysis. Patients should be managed in the hospital. Oral overdose is unlikely to cause toxicity since the drug is poorly absorbed.
7. Recommended medical monitoring:
 - a. Audiometric measurements and assessment of vestibular function prior to initiation of therapy and at regular intervals during treatment.
 - b. Weekly tests of renal function.
 - c. Frequent serum potassium levels.

Periodic Screening for Tuberculosis Infection

Periodic tuberculin skin test screening is particularly important for certain groups, including school children, residents or patients of long-term care facilities, persons in select occupational and other groups, and newly arrived immigrants (especially those from areas with high tuberculosis prevalence rates).

Tuberculin skin test screening is useful for the following purposes:

1. to identify persons with tuberculosis disease in order to prevent transmission;
2. to identify persons who may benefit from treatment of latent tuberculosis infection;
3. to provide information about the prevalence of tuberculosis infection in certain groups;
4. to evaluate current tuberculosis control strategies; and
5. to provide information for development of future tuberculosis control strategies.

Screening of school children

Periodic tuberculin skin testing of school children is required by Alaska law which states, *“Each public school district and non-public school offering pre-elementary education through the 12th grade, or a combination of these grades, shall administer an intradermal purified protein derivative (PPD) skin test for tuberculosis within 90 days of enrollment to each child who enrolls in*

- (1) grades kindergarten and seven; or*
- (2) the district in grades kindergarten or higher for the first time” (27 AAC 27.213).*

In addition, the Tuberculosis Control Program requires that students in all grades be skin tested annually at schools in which the majority of students are Asian or Alaska Native

(these groups have the highest risk of tuberculosis in Alaska) and at schools in which the prevalence rate of tuberculosis infection exceeds 1%. Schools required to test students in all grades are notified in writing by the Tuberculosis Control Program.

Tuberculin skin testing of school children is done by public health nurses at schools which lack personnel capable of conducting the testing. The school district is responsible for obtaining a consent form signed by the child’s parent or guardian prior to administration of a tuberculin skin test to a child in the parent’s absence. All children with undocumented or previously negative tuberculin reactions should be skin tested. Prior BCG vaccination is not a contraindication to tuberculin skin testing. The only exception to testing is if a physician provides a written statement that the test *“... would be injurious to the health and welfare of the child or members of the family or household” (27 AAC 27.213).*

The follow-up of tuberculin reactors ≤ 6 years of age and of tuberculin converters (of any age) should include an associate investigation (see pages 55-56). A public health nurse should ensure follow-up of children with positive tuberculin reactions who are reported to them by a school nurse or the Tuberculosis Control Program.

Skin testing of school children is required to be done by the Mantoux (PPD) method (27 AAC 27.213). Multiple-puncture tests have been found to be less sensitive and specific than Mantoux testing. The American Academy of Pediatrics stated that multiple-puncture tests are “not recommended” and the U.S. Centers for Disease Control and Prevention and the American Thoracic Society said that they are “not sufficiently accurate and should not be used.” [MMWR 2000; 49(RR-6):23. American

Academy of Pediatrics. In: Pickering LK, ed. 2000 Red Book: Report of the Committee on Infectious Diseases, 25th ed]. Most experts state that multiple-puncture tests are of limited or no value (Pediatr Infect Dis J 1995;14:455-70. Clin Infect Dis 1993;17:968-75).

Screening of immigrants

Most persons who apply for immigration to the United States are evaluated for infectious tuberculosis disease before leaving their country of origin by being screened with a chest x-ray. Those with an abnormal film compatible with active disease must then submit three sputum specimens for acid-fast bacilli smears. Smear negative persons are cleared for immigration while those who are smear positive must be treated until becoming smear negative before they are permitted entry to the U.S. Certain classes of immigrants are not subject to medical evaluation and may enter and reside in the U.S. without tuberculosis clearance.

These procedures are intended to exclude most persons with infectious tuberculosis from entering the country. However, they do not exclude applicants who either are smear negative, but who would have a positive culture (if a culture would have been done), or who have a chest x-ray interpreted as showing no active disease but who would have smear or culture positive disease if sputum had been examined. Likewise, immigrants not subject to medical evaluation may be infectious. Thus, it is critical that immigrants receive appropriate follow-up after arrival in the U.S.

Persons with an abnormal chest x-ray have the condition noted on their visa and are informed that they must be seen by the local health department after arrival. The Division of Quarantine at the U.S. Centers for Disease Control and Prevention notifies the Alaska Tuberculosis Control Program that such a person has arrived in Alaska. Immigrants with a

past or current history of tuberculosis are instructed to report to a health-care provider for follow-up within 30 days of their arrival in the U.S. If a health center is designated as an immigrant's planned source of follow-up, its staff usually receive a copy of the person's immigration report.

Screening of occupational and other groups

Alaska law requires annual tuberculosis clearance for persons in certain occupational categories, as follows:

1. school employees;
2. employees of health-care facilities licensed under Title 7, Chapter 12 of the Alaska Administrative Code (general acute care hospitals, specialized hospitals, nursing homes, intermediate-care facilities for the mentally retarded, ambulatory surgical facilities, birth centers, mental health centers, home health agencies); and
3. school bus drivers.

"Tuberculosis clearance" is defined in the regulations that apply to each group; such clearance usually involves tuberculin skin testing (if appropriate), evaluation for signs or symptoms of tuberculosis disease, and determination of tuberculosis risk factors. The employee should know his or her tuberculin skin test status and is responsible for providing proof of tuberculosis clearance to the appropriate agency or employer.

In 1996, regulations requiring tuberculin skin testing in certain other groups were repealed. These groups included careproviders at residential adult or child-care facilities, certain persons living in residential child-care facilities, foster parents, certain members of foster households, and careproviders and adult residents of adult foster homes.

Institutional screening

The Tuberculosis Control Program recommends annual screening for the following groups:

1. staff of acute health-care facilities (general hospitals and some psychiatric hospitals);
2. staff and residents of long-term care institutions (nursing homes, prisons, chronic disease hospitals, and other specialized patient care facilities);
3. staff of facilities or institutions (schools, nurseries, day care centers, etc.) where, if staff develop disease, there is potential for infecting large numbers of susceptible persons.

When annual (or other periodic) tuberculin skin test screening is to be done, the Mantoux (PPD) skin test should be used. When adults are screened for the first time, those who do not have a positive reaction should be retested 1 to 2 weeks later to identify boosting following the first test (see pages 24-25). This procedure will prevent the possibility that such persons would be incorrectly considered converters in subsequent periodic testing. After initial testing and follow-up is completed, the need for periodic testing should be assessed according to the risk of exposure to tuberculosis and specific regulations applying to the institution.

Persons being admitted to long-term care institutions who have a positive skin test (i.e., ≥ 10 mm induration) and who have not had a recent chest x-ray (within 1 month of admission) should have a chest x-ray [MMWR 1990:39(RR-10);7-20]. A person who develops protracted cough or fever or who has abnormal chest x-ray findings compatible with tuberculosis, especially if there is a significant skin test reaction, should be evaluated further (with sputum specimens for acid-fast bacilli smear and mycobacterial culture) to exclude tuberculosis.

The Public Health Nurse's Role in Tuberculosis

The following section describes the responsibilities and activities of public health nurses in the Alaska Division of Public Health related to tuberculosis control. Although local health departments and Alaska Native health corporations may delegate these responsibilities differently, this section can serve as a guide to these agencies for organizing and evaluating the range of tuberculosis control activities they conduct.

Health education

Public health nurses are responsible for teaching clients about tuberculosis, transmission of tuberculosis, its treatment, common side-effects of medicines used to treat tuberculosis, and the importance of compliance with recommended therapy. In addition, they provide information to other health-care providers, community organizations, and other institutions.

Reporting

Public health nurses should report to the Tuberculosis Control Program any confirmed or suspected cases of tuberculosis of whom they become aware or for whom they provide nursing care; this is required by Alaska law (7 AAC 27.005).

Tuberculin skin testing of school children

Alaska law requires that children at specific grade-levels be tuberculin skin tested within 90 days of enrollment in school. In many rural school districts, public health nurses ordinarily conduct the required annual tuberculin skin test screening of school children. They may also provide this service in some other schools without personnel capable of doing the screening. Results of the tuberculin screening should be provided to the appropriate school

personnel by the public health nurse. The school is responsible for submitting a completed "School Tuberculin Testing Report" (Form 41, pages 110-112) to the Tuberculosis Control Program. Public health nurses should not send a "Group Preventive Services" form to the Tuberculosis Control Program. Public health nurses should help to ensure that school-aged tuberculin reactors or converters are promptly evaluated and treated.

Contact and associate investigations

Public health nurses are responsible for doing contact and associate investigations. Contacts of every case of tuberculosis disease (whether pulmonary or extrapulmonary) must be evaluated by means of a contact investigation using the "concentric circle" approach. The public health nurse should begin this investigation as soon as possible after being notified of a suspected or confirmed case of tuberculosis disease unless Tuberculosis Control Program staff determine that an investigation is unnecessary or can be delayed temporarily. In addition, associates of tuberculin converters and of tuberculin reactors ≤ 6 years of age should be evaluated in an effort to identify the source of infection.

Initial and final results of contact or associate investigations must be forwarded to the Tuberculosis Control Program (see "Record of Examination of Close Contacts of Active Case or Associates of Recent Converter," pages 104-105). The results of the initial epidemiologic investigation should be recorded on a "Record of Examination of Close Contacts of Active Case or Associates of Recent Converter" and forwarded to the Tuberculosis Control Program no later than 30 days from the date of notification of the case to be investigated. Tuberculosis Control Program staff will contact the public health nurse at 30 days to see that

the investigation is complete. The results of the follow-up skin tests should also be reported on a copy of the record and forwarded to the Tuberculosis Control Program.

Monitoring treatment

Public health nurses are responsible for monitoring the medication compliance of persons in their jurisdiction who are prescribed anti-tuberculosis drugs. Although clients themselves are primarily responsible for notifying their medical providers about possible medication side-effects and for presenting themselves for medical follow-up, the public health nurse should help to ensure that changes in the client's health status are reported to the medical provider and that the client complies with recommended follow-up. If financial considerations prevent a client from seeking medical evaluation for tuberculosis, the public health nurse should consult with the Tuberculosis Control Program.

1. Ordering medicines: Public health nurses are responsible for ordering medicines from the Tuberculosis Control Program for clients receiving anti-tuberculosis drugs from public health centers, village clinics, or directly observed therapy aides.
2. Health education: As early in the course of therapy as possible (if not prior to the start of therapy), the public health nurse should discuss with the client the most common side-effects of the medicines being prescribed. Ultimately, however, this is the responsibility of the client's medical provider. The client should be advised to report possible side-effects to their medical provider.
3. Administration of medicines: Public health nurses are responsible for organizing and managing directly observed therapy (DOT). These responsibilities include identifying, hiring, training, and working with DOT aides as well as setting-up appropriate incentives and

enablers for the client. DOT calendars should be submitted by the DOT aide through the public health nurse to the Tuberculosis Control Program for payment of services.

4. Client assessment: On a monthly basis, the public health nurse should question the client about the presence of adverse reactions associated with the medicines being taken (see Table 7, page 60) and about any changes in health. A brief physical assessment should be done to identify any signs of medication-associated side-effects. For example, it may be appropriate to weigh the client or take an oral temperature, to check for jaundice or scleral icterus in clients taking isoniazid or rifampin, or to test visual acuity and color vision in clients taking ethambutol. Appropriate periodic physical assessment and follow-up are also the responsibility of the client's health-care provider. The public health nurse may agree, at the provider's request, to perform specific assessments if the public health nurse is able to do so. The public health nurse should send to the client's health-care provider a copy of the record of each encounter with the client and should promptly report any substantial changes in the client's health.
5. Information reporting: For clients who were started on treatment of latent tuberculosis infection and who have finished or discontinued therapy, the public health nurse should complete the "Patient Surveillance Report" (pages 106-107) which is distributed by the Tuberculosis Control Program every 3 months. For clients being treated for tuberculosis disease, the public health nurse should notify Tuberculosis Control Program staff of the date on which treatment is completed.
6. Follow-up of clients receiving anti-tuberculosis therapy: The public health nurse should help to ensure that any follow-up recommended by the client's medical provider

is carried out. In addition, the public health nurse should ensure that, beginning 2 weeks after therapy is started, every client who was initially sputum smear or culture positive submit three sputum specimens for mycobacterial culture each month until all specimens from a monthly collection are negative. One or 2 weeks after the completion of treatment, the public health nurse should ensure that a series of three sputum specimens are collected for mycobacterial culture.

7. Clients who relocate or travel: Public health nurses should notify the Tuberculosis Control Program as soon as they become aware that a person being treated for tuberculosis disease or latent tuberculosis infection is planning to or has changed locations. Tuberculosis Control Program staff will notify public health nurses in the new location of the client's situation.

Screening of clients

Clients may present themselves to a public health nurse in order to be screened for evidence of latent tuberculosis infection or disease. The public health nurse should skin test persons with unknown or previously negative skin test results. Tuberculin-positive persons should be assessed for signs or symptoms of tuberculosis and for tuberculosis risk factors, and referred for medical evaluation, if indicated.

Specific activities conducted by public health nurses

1. Patient Surveillance Reports:

Every 3 months, the Tuberculosis Control Program distributes a "*Patient Surveillance Report*" (pages 106-107) for each client who should have recently completed treatment of latent tuberculosis infection. If the client has completed or discontinued treatment, the report should be completed and returned promptly to the Tuberculosis Control Program.

The beginning and ending dates of treatment must be specified on the report. An estimate of the client's compliance is not necessary. The public health nurse should indicate whether the client completed or did not complete treatment, and if the client did not complete therapy, the reason for discontinuation of therapy should be indicated. The primary medical provider's responsibilities include evaluating the client prior to therapy, providing written prescriptions for the client's medicine(s), and ordering and conducting appropriate follow-up (including biochemical and other monitoring) of the client during treatment.

2. Ordering medicine:

a. Treatment of latent tuberculosis infection (LTBI) - Public health nurses may distribute 30-tablet containers of isoniazid 300 mg from their stock supply after a health-care provider has written a prescription. Orders for other LTBI treatment drugs or for isoniazid dosages other than 300 mg should be sent by mail to the Tuberculosis Control Program after a health-care provider has prescribed the treatment regimen. Fill out a "*Drug Order and Refill Request*" (Form 10, pages 102-103) and mail it to the Tuberculosis Control Program, allowing 2 weeks for delivery. No more than a 3-month supply of medicine should be ordered at one time. Medicines can be sent to the public health nurse, who in turn either gives them to the client at a clinic or home visit or sends them to the client's village health aide or to the directly observed therapy (DOT) aide. If a client does not wish - or cannot afford - to have a private provider prescribe treatment, Tuberculosis Control Program staff may be willing to prescribe the treatment regimen.

b. Tuberculosis disease - On receipt of a prescription for medicines for a client who is beginning multidrug anti-tuberculosis therapy, the public health nurse should telephone the Tuberculosis Control Program to request a 3-

month supply of medicines for the patient. Medicines may be ordered by mail or by fax. If an order is sent by fax, a copy clearly marked "copy of faxed order" should be sent by mail. For clients who are continuing anti-tuberculosis therapy, the public health nurse should fill out a "Drug Order and Refill Request" (Form 10, pages 102-103) and send it to the Tuberculosis Control Program soon enough to allow 2 weeks for delivery. Public health nurses may dispense Rifamate 2 caps/day (or the equivalent: isoniazid 300 mg and rifampin 600 mg) from the stock supply. Additional medicines can be started when they arrive from the Tuberculosis Control Program.

c. Stock medications - Stock supplies of isoniazid 300 mg tablets and Rifamate capsules may be ordered on a Form 10 by writing "stock" in the space for the client's name. The completed form should be mailed (not faxed) to the Tuberculosis Control Program. Any unused medicine should be returned to the Tuberculosis Control Program at least 4 months prior to its expiration date. The public health nurse should dispense medicines to the patient only on verbal or written order from the prescribing health-care provider. The public health nurse should have received, within 1 month of starting the client's treatment, a written prescription for the medicines from the client's physician. The original prescription should be kept in the client's record or chart.

3. Exchange of client information:

The public health nurse should have the client sign a "Release of Medical Information" form (page 114) at the first contact with the client. (Although tuberculosis is a reportable disease thus requiring health-care providers to release information to the Tuberculosis Control Program, obtaining a signed medical release form may expedite requests for information.) Public health nurses should send the Tuberculosis Control Program a copy of records of encounters with clients with

suspected or confirmed tuberculosis disease. Copies should also be sent to the client's health-care provider. Information from these records will be used to update clinical data in the tuberculosis case registry. New information essential to the client's care which comes to the attention of the Tuberculosis Control Program staff will be communicated to the public health nurse by telephone, by letter, or on a "Clinical Summary/Update/Chest X-ray Interpretation" form. In addition to clinical summaries or x-ray interpretations, the "Clinical Summary/Update/Chest X-ray Interpretation" form may contain recommendations for submitting mycobacterial cultures or conducting contact (or associate) investigations.

The public health nurse should record the date on which the client completes all prescribed anti-tuberculosis therapy and should notify Tuberculosis Control Program personnel of the date of completion. If a client stops taking medicines before completing a full course of anti-tuberculosis therapy, then the date on which medicines were stopped and the reason for stopping should be reported to the Tuberculosis Control Program.

Although public health nurses are not responsible either for fully evaluating clients for tuberculosis or for establishing the diagnosis of tuberculosis, they may be asked by health-care providers or by the Tuberculosis Control Program to perform, or facilitate the performance of, certain procedures. These procedures might include: Mantoux (PPD) skin-testing; obtaining a history from a client for signs or symptoms of tuberculosis disease and for tuberculosis risk factors; collecting sputum specimens for acid-fast bacilli smears and mycobacterial cultures; or arranging for a client to have a chest x-ray or other test.

4. Assessment activities:

The public health nurse should collect sputum specimens from clients for acid-fast bacilli smear or mycobacterial culture if asked to do so by the client's medical provider or the Tuberculosis Control Program. A public health nurse may also obtain sputum specimens for mycobacterial culture from clients found to have substantial, persistent respiratory symptoms possibly indicative of tuberculosis; and the public health nurse should report this information to the client's health-care provider. Sputum cultures should not be used merely as a screening tool for asymptomatic clients.

Public health nurses are expected to conduct contact and associate investigations in order to determine whether contacts of persons with potentially infectious tuberculosis disease are infected and to evaluate associates of certain persons with latent tuberculosis infection (see pages 55-58).

Public health nurses will assess tuberculosis clients, at monthly intervals, for any changes in their health. This brief assessment should be directed at detecting any medication-related side-effects and improvement or worsening of their tuberculosis disease. In the case of a client who receives medicines from a village health aide or directly observed therapy aide, the public health nurse should periodically obtain information about the client's health status. Any new health problems should be reported to the client's health-care provider. The public health nurse should help to ensure that the case-responsible medical provider's orders for biochemical monitoring (e.g., liver function tests) or other periodic testing for medication-associated side-effects are carried out. Public health nurses may obtain liver function tests for clients meeting the criteria given on pages 33 and 50; they should consult with Tuberculosis Control Program staff for questions about testing persons not covered by the criteria.

Clients' compliance with therapy should be assessed periodically. Most or all persons being treated for tuberculosis disease will be placed on directly observed therapy (DOT); their compliance can easily be determined. For the rare client not on DOT, compliance can only be determined by indirect means. Compliance can be assessed by noting the dates on which medicines were picked up by the client, counting the number of pills remaining in medicine containers, or observing the color of urine of patients taking rifampin (it should be orange-pink). The public health nurse must notify Tuberculosis Control Program staff immediately if a patient appears to be non-compliant (that is, if patient interrupts therapy or fails either to begin or to continue therapy).

Appropriate therapy should result in rapid conversion of sputum cultures to negative. For clients whose initial sputum smears or cultures are positive, the public health nurse should collect three sputum specimens for smear and mycobacterial culture monthly (beginning 2 weeks after therapy is started) until all cultures from a single month's collection are negative. If cultures continue to be positive after the third month of anti-tuberculosis treatment, the client should be reassessed by their health-care provider to determine if they failed to comply with recommended therapy or if their tuberculosis organisms have developed antibiotic resistance.

5. Screening and follow-up of new immigrants:

Public health nurses may have a role in screening new immigrants for evidence of tuberculosis and insuring that appropriate follow-up is recommended. Public health centers are periodically sent reports concerning new immigrants by the Division of Quarantine of the U.S. Centers for Disease Control and Prevention. Reports should be

retained for at least 2 weeks to allow the immigrant time to appear.

If the immigrant does not appear within 2 weeks, a letter should be sent by a public health nurse to encourage the person to make an appointment for follow-up. He or she should be asked to bring their immigration chest x-ray to the center. The public health nurse should review any reports accompanying the chest x-ray and the immigrant should be questioned about past exposure to tuberculosis, signs or symptoms of pulmonary tuberculosis, tuberculosis risk factors, history of BCG vaccination, history of treatment for tuberculosis infection or disease, and tuberculin skin test history (see pages 98-99). Unless there is a documented history of culture-confirmed tuberculosis or a documented history of a significant Mantoux (PPD) reaction, a Mantoux skin test should be placed. If the immigrant is taking medicines for tuberculosis disease, the public health nurse should contact Tuberculosis Control Program staff immediately. If the immigrant will run out of anti-tuberculosis medicine before being seen by a physician, in consultation with the Tuberculosis Control Program, the public health nurse may provide the client with enough medicine to last until then.

The public health nurse should have the immigrant obtain a chest x-ray only if: (a) the person is classified as having current tuberculosis disease, (b) the person has evidence of latent tuberculosis infection and the most recent chest x-ray is more than 2 months old, or (c) the Tuberculosis Control Program recommends that one be obtained. The public health nurse should obtain three sputum specimens (one of which is observed) for mycobacterial culture if the immigrant has respiratory symptoms compatible with tuberculosis and is able to produce sputum spontaneously.

A copy of the immigrant's encounter at the health center, as well as accompanying records, should be forwarded to Tuberculosis Control Program staff, who will report to the Division of Quarantine of the U.S. Centers for Disease Control and Prevention. The Tuberculosis Control Program will send to the public health nurse recommendations for any further follow-up of the immigrant.

Non-responsibilities

Public health nurses' responsibilities in tuberculosis control do not include the following:

1. Prescribing therapy or, without a medical provider's order, initiating therapy.
2. Altering therapy (unless ordered to do so by the case-responsible medical provider).
3. Prescribing or determining the nature of medical follow-up of clients, or conducting medical follow-up.
4. Diagnosing tuberculosis.
5. Recommending or requesting diagnostic procedures.

Appendix 1. Statutes and Regulations

The following section contains statutes and regulations relevant to tuberculosis control in Alaska. This material was current as of February 2001.

Statutes

Alaska Statute Sec. 18.15.120.

TUBERCULOSIS CONTROL PROGRAM AUTHORIZED.

The department may establish a comprehensive program for the control of tuberculosis in the state, and may

- (1) arrange means by which persons in the state may be X-rayed to determine the presence of tuberculosis;
- (2) establish necessary out-patient clinics for the care of tuberculosis;
- (3) encourage and promote the establishment of adequate health care facilities within the state to care for persons suffering from tuberculosis and allied conditions;
- (4) under the provisions of AS 36.30 (State Procurement Code), obtain, by purchase or donation from surplus federal property or otherwise, medical supplies and equipment useful in carrying out this program and allot or resell these supplies and equipment to private institutions engaged by the department to carry out this program;
- (5) under the provisions of AS 36.30, contract with hospitals, associations, or other health care facilities qualified and equipped to give adequate care inside or outside the state;
- (6) employ necessary and trained personnel to carry out the purposes of AS 18.15.120 - 18.15.149;
- (7) pay the costs of care and incidental expenses for residents of the state, in whole or in part, depending on the ability of each

patient to pay, and the temporary costs of care and transportation for nonresidents on the same basis until they can be transferred to their residence;

- (8) enlist the cooperation of state, federal, and local agencies operating in the state for the furtherance of this program;
- (9) establish standards in accordance with department procedure for the care of persons with tuberculosis receiving treatment under AS 18.15.120 - 18.15.149;
- (10) adopt regulations to implement and interpret AS 18.15.120 - 18.15.149.

Alaska Statute Sec. 18.15.130.

DEPARTMENT TO COOPERATE WITH OTHER AGENCIES.

The department, in establishing a comprehensive program for the control of tuberculosis in the state, shall cooperate with state, federal, and local agencies operating in the state, and obtain as much information and data as possible from them.

Alaska Statute Sec. 18.15.131.

REPORTS TO STATE MEDICAL OFFICERS; DOCUMENTATION OF TREATMENT.

- (a) A health care provider and a laboratory administrator shall report, within five working days, to a state medical officer when that provider or administrator diagnoses a case of tuberculosis or has reasonable grounds to believe that a patient has tuberculosis, or when a patient ceases treatment for tuberculosis. A health care provider and a laboratory administrator may presume that a patient has ceased treatment if the patient fails to keep an appointment or relocates without transferring medical treatment to another health care provider. A health care provider who treats a patient with tuberculosis, and a person in

charge of a health care facility that provides treatment for tuberculosis to a patient, shall maintain written documentation of the patient's adherence to the patient's treatment plan.

(b) A person required to report under (a) of this section shall permit a state medical officer to examine patient records, reports, and other data related to the required report.

Alaska Statute Sec. 18.15.133.

EXAMINATION OF PERSONS EXPOSED TO TUBERCULOSIS.

(a) A health care provider who treats a patient for tuberculosis shall

- (1) examine all other persons in the household who have had contact with the patient;
- (2) refer those persons to another health care provider for examination and notify the other health care provider and a state medical officer of the referral; or
- (3) refer those persons to a state medical officer for examination and promptly notify the state medical officer of the referral.

(b) A health care provider who examines other persons in a household under (a)(1) or (2) of this section shall report to a state medical officer, within 10 days after the examination, the results of the examination.

(c) Under AS 18.15.135, a state medical officer may order an examination of a person to detect tuberculosis, for the purpose of directing preventive measures for the person, if the state medical officer has reasonable grounds to believe that the person is at heightened risk of exposure to tuberculosis.

Alaska Statute Sec. 18.15.135.

TUBERCULOSIS EXAMINATIONS.

(a) A person shall submit to an examination to detect tuberculosis whenever, in the opinion of a state medical officer, an examination is necessary to preserve and protect public health.

(b) An examination under this section shall be by written order issued by a state medical officer that must specify the name of the person to be examined and the time and place of the examination. The person to be examined shall be personally served with a copy of the order within a reasonable period of time before the examination is to take place.

(c) An examination under this section shall be performed by a physician who may lawfully practice in the state. The person to be examined may, under conditions specified by the state medical officer, choose the physician who will perform the examination.

Alaska Statute Sec. 18.15.136.

ADDITIONAL ORDERS TO PROTECT THE PUBLIC HEALTH.

(a) In addition to orders issued under AS 18.15.135, if a state medical officer determines that the public health in general, or the health of a particular person, is endangered by exposure to a person who is known to have tuberculosis, or by exposure to a person for whom there are reasonable grounds to believe has tuberculosis, a state medical officer may issue the orders that the medical officer finds necessary to protect the public from a threat to the public health. An examination ordered under this section shall be performed by a physician who may lawfully practice in the state. Under conditions specified by the state medical officer who issued the order, the person to be examined may choose the physician who will perform the examination. A state medical officer may not under this

section order the forcible or involuntary administration of medicine. The state medical officer, through the Department of Law, may make application to a court for enforcement of an order issued under this section.

(b) An order issued under (a) of this section may include

(1) an authorization for the removal to or admission into a health care facility for appropriate examination for infectious tuberculosis of a person who is known to have tuberculosis, or of a person for whom there are reasonable grounds to believe that the person has tuberculosis and who is unable or unwilling to submit to an examination ordered under AS 18.15.135;

(2) a requirement that a person who has tuberculosis complete an appropriate treatment plan for tuberculosis and, if necessary, follow required infection control precautions for tuberculosis;

(3) a requirement that a person be removed to, admitted into, and subsequently detained in, a health care facility, if

(A) the person has infectious tuberculosis, or presents a substantial likelihood of having infectious tuberculosis, based upon epidemiologic information, clinical findings, X-ray readings, or tuberculosis laboratory test results; and

(B) the state medical officer finds that a substantial likelihood exists that the person may transmit tuberculosis to others because of the person's inadequate separation from others;

(4) a requirement that a person be removed to, admitted into, and subsequently detained in a health care facility for treatment if

(A) the person has infectious tuberculosis, or has been reported to a state medical officer as having infectious tuberculosis, and the state medical officer has no knowledge that the person has completed an appropriate treatment plan for tuberculosis; and

(B) substantial likelihood exists, based on the person's past or present behavior, that the person cannot be relied upon to participate in or complete an appropriate treatment plan for tuberculosis or, if necessary, follow required infection control precautions for tuberculosis; the state medical officer may consider as indicators of unreliability the person's refusal or failure to take medication for tuberculosis, refusal or failure to keep appointments for treatment for tuberculosis, refusal or failure to complete a treatment plan for tuberculosis, or disregard for infection control precautions prescribed by a health care provider or a state medical officer;

(5) an authorization for isolation of a person with infectious tuberculosis through detention at the person's place of residence until the state medical officer has determined that the person no longer has infectious tuberculosis.

(c) A state medical officer shall issue an order under this section in writing, and in the order shall set out the following:

(1) the name of the person required to comply with the order, the period of time during which the order is in effect, and other terms and conditions that the state medical officer determines to be necessary to protect the public health;

(2) the legal authority under which the order is issued;

(3) an assessment of the person's circumstances or behavior constituting the basis for the issuance of the order; and

(4) any less restrictive treatment alternatives that were attempted and were unsuccessful, or less restrictive treatment alternatives that were considered and rejected, and the reasons for the rejection of those alternatives.

(d) In addition to the requirements of (c) of this section, an order for the detention of a person must include

(1) the purpose of the detention;

(2) advice to the person being detained that the person has the right to request release from detention by contacting the state medical officer at the telephone number stated on the order and that, under AS 18.15.139, in the absence of a court order authorizing the detention, the detention may not continue for more than five business days after the request for release;

(3) advice to the person being detained that, under AS 18.15.139, the state medical officer is required to obtain, within 60 days following the commencement of detention, a court order authorizing the detention and after that must seek further court review of the detention within 90 days after the court order and within 90 days after each subsequent court review;

(4) advice to the person being detained that the person has the right to arrange to be represented by counsel or, under AS 18.85.100, to have court-appointed counsel provided; and

(5) advice to the person being detained that the person has the right to elect whether a proceeding providing court review is open or closed to the public.

(e) A state medical officer is not required to obtain a court order before issuing an order under this section for detention of a person.

Alaska Statute Sec. 18.15.137.

EMERGENCY DETENTION ORDERS.

A state medical officer, through the Department of Law, may request the court to issue an order for the emergency detention of a person when the state medical officer finds that a substantial likelihood exists that the person has infectious tuberculosis in order to prevent the person from posing a threat to the public health. Upon issuance of an ex parte court order, a peace officer or a state medical officer shall take the person into custody and deliver the person to the nearest available health care facility or another location that will provide for the protection of the public health. The state medical officer, through the Department of Law, shall make application for a court order authorizing continued detention of the person within 72 hours after the issuance of an ex parte order or, if the 72-hour period ends on a Saturday, Sunday, or legal holiday, by the end of the first state working day following the Saturday, Sunday, or legal holiday. The court shall schedule a hearing within five state working days after receipt of an application for authorization of continued detention.

Alaska Statute Sec. 18.15.139.

COURT AUTHORIZATION OF DETENTION.

(a) If a person detained under an order issued under AS 18.15.136 requests release from detention, the state medical officer shall make an application for a court order authorizing continued detention within 72 hours after the request or, if the 72-hour period ends on a Saturday, Sunday, or legal holiday, by the end of the first state working day following the Saturday, Sunday, or legal holiday. The court shall schedule a hearing within five state working days after receipt of the state medical

officer's application. After a detained person requests release, detention of that person may not continue for more than five business days in the absence of a court order authorizing continued detention. However, no person may be detained under an order issued under AS 18.15.136 for more than 60 days without a court order authorizing the detention. A state medical officer, through the Department of Law, shall seek further court review of a detention within 90 days following the initial court order authorizing the detention and within 90 days after each subsequent court order authorizing detention.

(b) In a court proceeding to authorize or enforce a state medical officer's order under AS 18.15.136 for the detention of a person, the state medical officer must prove the circumstances constituting the necessity for the detention by clear and convincing evidence.

(c) A person who is subject to a detention order under AS 18.15.136 has the right to be represented by counsel or to have, under AS 18.85.100, court-appointed counsel provided.

(d) A person who is the subject of a court proceeding initiated under AS 18.15.136 or 18.15.137 may elect to have the hearing open or closed to the public.

Alaska Statute Sec. 18.15.143.

RELIGIOUS TREATMENT FOR TUBERCULOSIS.

(a) If a person with infectious tuberculosis establishes that that person is being provided treatment for tuberculosis by spiritual means or establishes that the person's sincerely held religious beliefs prohibit medical treatment, a state medical officer or the court, in issuing an order under AS 18.15.136, 18.15.137, or 18.15.139, may consider the spiritual treatment or religious beliefs as well as the health of the person and may order that the person only be

isolated at the person's home, or other suitable place of the person's choice, in a manner that will protect the public health.

(b) A person with infectious tuberculosis who is or might become subject to an order issued under AS 18.15.136, 18.15.137, or 18.15.139, at any time may request recognition and consideration of spiritual treatment or religious beliefs as described in (a) of this section.

(c) In this section, "spiritual means" means prayer, or a substantially similar activity, by an established practitioner of a recognized church or religious denomination, in accordance with the tenets and practices of that church or religious denomination.

Alaska Statute Sec. 18.15.145.

SCREENING OF SCHOOL EMPLOYEES.

(a) An employee of a public or private elementary or secondary school in the state shall be tested annually to detect infectious tuberculosis. An employee who has never had a positive test result from a tuberculin skin test shall obtain a tuberculin skin test. An employee whose skin test result is positive or who has ever had a positive skin test result shall have an appropriate health screening examination that may include obtaining a chest X-ray.

(b) An employee who refuses or fails to be tested as required under (a) of this section is suspended from employment until the employee has been tested.

(c) The school district annually shall obtain from each school employee in the district a certificate or other evidence that the employee has been tested as required in (a) of this section.

(d) The department may by regulation provide for reasonable exceptions to the requirements of this section.

Alaska Statute Sec. 18.15.147.

LIMITED IMMUNITY.

A person may not bring an action for damages based on the decision under AS 18.15.120 - 18.15.149, to detain or not to detain a person unless the action is for damages caused by gross negligence or intentional misconduct.

Alaska Statute Sec. 18.15.149.

DEFINITIONS.

In AS 18.15.120 - 18.15.149,

- (1) "department" means the Department of Health and Social Services;
- (2) "division of public health" means the division of public health in the department;
- (3) "health care facility" means a hospital, specialty hospital, long-term care facility, medical clinic, or similar facility for which a license has been issued by this state and in which inpatient or outpatient medical services for tuberculosis are provided;
- (4) "health care provider" means an acupuncturist, nurse, nurse practitioner, pharmacist, physician, or physician's assistant, hospital, or health clinic who may lawfully practice in this state;
- (5) "state medical officer" means a physician employed by the division of public health;
- (6) "tuberculosis" means a disease caused by mycobacterium tuberculosis, mycobacterium bovis, or mycobacterium africanum.

Regulations

4 Alaska Administrative Code (AAC) 60.100.
PHYSICAL EXAMINATION FOR CHILDREN.

(Note: This section applies to children in pre-elementary school.)

(a) Not more than three months before first entering school, each child must have a

tuberculosis skin test which meets the requirements of 7 AAC 27.213.

(b) Before first entering school, each child must have received the immunizations required by 4 AAC 06.055.

4 AAC 60.115.

STAFF.

(Note: This section applies to pre-elementary schools.)

(a) All staff members must have a physical examination not more than three months before initial employment and every three years after that. It is the responsibility of the operator to maintain a personnel file for each employee, in which the results of the current physical examination must be kept. This file is subject to inspection by the department.

(b) All employees and volunteers who work in the classroom or who provide direct services to children in the pre-elementary school shall be evaluated annually, except as provided otherwise in this subsection, to detect active cases of pulmonary tuberculosis, as follows:

- (1) a person who has never had a positive tuberculin skin test result shall obtain a tuberculin skin test;
- (2) a person who has previously had a positive tuberculin skin test result, or a person whose tuberculin skin test obtained under (1) of this subsection has a positive result,
 - (A) shall have a health evaluation by a health care provider to identify symptoms suggesting that tuberculosis disease is present; the health evaluation must also include evaluation for the presence of any of the following risk factors: evidence of inadequately treated past tuberculosis disease, history of close exposure to a case of communicable pulmonary tuberculosis

within the previous two years, history of a negative tuberculin test within the previous two years, diabetes mellitus (severe or poorly controlled), diseases associated with severe immunologic deficiencies, immunosuppressive therapy, silicosis, gastrectomy, excessive alcohol intake, or human immunodeficiency virus infection; if symptoms suggesting tuberculosis disease are present, or if any of the risk factors is present, a chest x-ray shall be obtained as part of the health evaluation and the health care provider shall report the case to the section of epidemiology, division of public health, Department of Health and Social Services; and

(B) if the person has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the person need not have further annual tuberculosis evaluation under this subsection.

(c) A school subject to the provisions of this chapter shall comply with all applicable statutes and regulations concerning labor and employment practices.

7 AAC 12.566.

INFECTION CONTROL.

(a) A home health agency shall develop and implement written policies and procedures applicable to all agency staff that

- (1) minimize the risk of transmitting infection in all patient care or services; and
- (2) provide for the safe handling and disposal of biohazardous and infectious materials.

(b) At least every two years, a home health agency shall verify that its employees, contractors, and volunteers who provide

patient care receive training on universal precautions and the prevention, transmission, and treatment of

- (1) human immunodeficiency virus (HIV);
- (2) acquired immunodeficiency virus (AIDS);
- (3) hepatitis; and
- (4) tuberculosis.

7 AAC 12.571.

EMPLOYEE HEALTH PROGRAM.

(a) Except as provided in (b) - (e) of this section, a home health agency shall have an employee health program that requires each employee to be tested for pulmonary tuberculosis within the first two weeks of initial employment and annually thereafter. The home health agency shall require contractors performing patient care or services for the agency to have similar standards in place.

(b) An employee who has never had a positive tuberculin skin test result must have a tuberculin Mantoux skin test. A further annual tuberculin testing [sic] is not necessary if the

- (1) test is negative;
- (2) employee is never required to be in a room where a patient or resident might enter; and
- (3) employee does not handle clinical specimens from a patient or other material from a patient's room.

(c) An employee who has a positive tuberculin skin test result, or previously had a positive tuberculin skin test result, must have a health evaluation to determine if tuberculosis disease is present. If the presence of tuberculin [sic] disease is confirmed, the employee shall be removed from direct contact with patients until the employee has received written verification from a physician that the employee is determined to be noncontagious.

(d) If the employee has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the employee need not have further annual tuberculosis evaluation.

(e) A home health agency that provides care to pregnant women shall document that each employee who provides direct patient care has been immunized against rubella by having on file

- (1) a valid immunization certificate signed by a physician or registered nurse listing the date of rubella vaccination;
- (2) a copy of a record from a clinic or health center showing the date of rubella vaccination; or
- (3) the result of a serologic test showing the employee is immune.

7 AAC 12.650.

EMPLOYEE HEALTH PROGRAM.

(Note: The term "facility" as used in 7 AAC 12.650 is defined in 7 AAC 12.990 to mean a general acute care hospital, specialized hospital, nursing home, intermediate care facility for the mentally retarded, ambulatory surgical center, birth center, mental health center, and home health agency.)

(a) Each facility must have an employee health program that

- (1) requires each employee to be evaluated within the first two weeks of employment and, except as provided otherwise in this paragraph, annually after that, to detect active cases of pulmonary tuberculosis, as follows:
 - (A) an employee who has never had a positive tuberculin skin test result shall obtain a tuberculin Mantoux skin test; if the tuberculin skin test result is negative, the employee does not need to have further annual tuberculosis

evaluation under this paragraph if the employee's duties never require him or her to be in a room where patients or residents might enter, and if the employee does not handle clinical specimens or other material from patients or from their rooms; an example of such an employee is an administrative person or research worker whose place of work is remote from patient or residential care areas and who does not come in contact with clinical specimens;

(B) an employee who has previously had a positive tuberculin skin test result, or an employee whose tuberculin skin test obtained under (A) of this paragraph has a positive result,

- (i) shall have a health evaluation by a health care provider to identify symptoms suggesting that tuberculosis disease is present; the health evaluation must also include evaluation for the presence of any of the following risk factors: evidence of inadequately treated past tuberculosis disease, history of close exposure to a case of communicable pulmonary tuberculosis within the previous two years, history of a negative tuberculin test within the previous two years, diabetes mellitus (severe or poorly controlled), diseases associated with severe immunologic deficiencies, immunosuppressive therapy, silicosis, gastrectomy, excessive alcohol intake, or human immunodeficiency virus infection; if symptoms suggesting tuberculosis disease are present, or if any of the risk factors is present, a chest x-ray shall be obtained as part of the health evaluation and the health

care provider shall report the case to the section of epidemiology, division of public health; and

(ii) if the employee has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the employee need not have further annual tuberculosis evaluation under this paragraph; and

(2) requires evidence of immunization against rubella by

(A) a valid immunization certificate signed by a physician listing the date of rubella vaccination;

(B) a copy of a record from a clinic or health center showing the date of vaccination; or

(C) the result of a serologic test approved by the department showing the employee is immune.

(b) The requirement of (a)(2) of this section does not apply to home health agencies, nursing homes, or ambulatory surgical facilities, and, for employees of other facilities, may be waived if a physician signs a certificate that there are medical reasons which dictate that an employee should not be vaccinated against rubella.

7 AAC 27.005.

REPORTING BY HEALTH CARE PROVIDERS.

(a) A health care provider who prescribes for or attends a person with one or more of the following infections or diseases must report any of the following infections or diseases of public health significance, if diagnosed or suspected by the health care provider: acquired immune deficiency syndrome (AIDS); amebiasis; anthrax; botulism; brucellosis; campylobacteriosis; chlamydia; cholera; cryptosporidium; cyclospora; diphtheria;

echinococcus; E. coli 0157:H7; giardiasis; gonorrhea; Haemophilus influenzae invasive disease; hepatitis (type A, B, or C); human immunodeficiency virus (HIV); legionellosis; leprosy; Lyme disease; malaria; meningococcal invasive disease; mumps; paralytic shellfish poisoning; pertussis; poliomyelitis; plague; psittacosis; rabies; Reye syndrome; rheumatic fever; rubella; rubeola; salmonellosis; shigellosis; syphilis; tetanus; trichinosis; tuberculosis; tularemia; typhoid fever; yellow fever; yersiniosis; severe reactions to a vaccination; epidemic outbreaks; an unusual incidence of infectious disease.

(b) The following infections or diseases are public health emergencies that must be immediately reported by the telephone directly to a public health official in the division of public health in the department when first diagnosed or suspected by the health care provider: anthrax; botulism; diphtheria; meningococcal invasive disease; paralytic shellfish poisoning; poliomyelitis; rabies; rubella; rubeola; tetanus.

(c) Except for an infection or a disease listed in (b) of this section, the health care provider must submit a report to the division orally, electronically, or on a form provided by the division within five working days after first discovering or suspecting the existence of the infectious disease or disease outbreak. Each report must give the name, address, age, sex, ethnicity, and race of the person diagnosed as having the reported infection or disease and the name and address of the health care provider reporting the infection or disease.

(d) Outbreaks or unusual incidences of diseases that are known or suspected to be related to exposure to environmental toxic or hazardous material must be reported by the physician, nurse, or other health care professional who prescribes for or attends those affected.

7 AAC 27.007.

REPORTING BY LABORATORIES.

(a) Public, private, military, hospital, or other laboratories performing serologic, immunologic, microscopic, biochemical, or cultural tests in this state or on samples obtained within this state must report evidence of human infection caused by the following agents at the time of identification or suspected identification: *Bacillus anthracis*; *Bordetella pertussis*; *Borrelia burgdorferi*; *Brucella abortus*; *Campylobacter* species; *Chlamydia psittaci*; *Chlamydia trachomatis*; *Clostridium botulinum*; *Clostridium tetani*; *Corynebacterium diphtheriae*; *Cryptosporidium* species; *Cyclospora*; *E. Coli* 0157:H7; *Echinococcus* species; *Entamoeba histolytica*; *Francisella tularensis*; *Giardia lamblia*; Invasive disease due to *Haemophilus influenzae*; hepatitis (A, B, or C virus); human immunodeficiency virus (HIV); influenza virus; *Legionella pneumophila*; measles virus; viral causes of meningitis; mumps virus; *Mycobacterium leprae*; *Mycobacterium tuberculosis*; *Neisseria gonorrhoeae*; *Neisseria meningitidis*; *Plasmodium* species; poliovirus; rabies virus; rubella virus; *Salmonella* species; *Shigella* species; *Treponema pallidum*; *Trichinella* species; *vibrio cholera*; yellow fever virus; *Yersinia enterocolitica* or *Y. pseudotuberculosis*; *Yersinia pestis*.

(b) Reports must be submitted to the division orally, electronically, or on a form provided by the division or on a legible copy of the original laboratory report form within five working days after the examination or test is performed. Each notification must give the date and result of the test performed, the name or identification code sufficient to identify the patient to the health care provider, and, when available, the age, sex, race, and ethnicity of the person from whom the specimen was obtained and the name and address of the health care

provider for whom the examination or test was performed.

(c) When acting on the basis of information received from laboratory notification, the division will not, except in instances of overriding public health considerations, contact the patient without first requesting the permission of the physician or other health care provider.

(d) Repealed 1/19/96.

(e) The following infectious agents are public health emergencies that must be reported immediately by telephone directly to a public health official in the division of public health when identified or suspected by the laboratory: *Bacillus anthracis*; *Corynebacterium diphtheriae*; measles virus; *Neisseria meningitidis*; poliovirus; rabies virus.

7 AAC 27.016.

RIGHT OF INSPECTION.

The division of public health may have access to any establishment and records of any establishment in the discharge of its official duties in accordance with law.

7 AAC 27.213.

TUBERCULOSIS SKIN TEST.

(Note: Skin test requirements for children in pre-elementary school are in 4 AAC 60.100.)

(a) Each public school district and non-public school offering pre-elementary education through the 12th grade, or a combination of these grades, shall administer an intradermal purified protein derivative (PPD) skin test for tuberculosis within 90 days of enrollment to each child who enrolls in

- (1) grades kindergarten and seven; or
- (2) the district in grades kindergarten or higher for the first time.

(b) The division may require a district or a non-public school to administer PPD skin tests to enrolled children in addition to those tests required under (a) of this section. The division shall issue a notice to a district or a non-public school requiring enrolled children in additional grade levels, including potentially all grade levels, to be PPD skin tested if the division makes a determination that there is evidence of increased risk of spread of tuberculosis in the community or communities where the district or the non-public school is located. The division shall use the following criteria to determine the need for additional required testing required under this subsection:

- (1) evidence that the results of prior PPD skin testing of school children in the local community or communities demonstrate tuberculosis transmission;
- (2) evidence that tuberculosis disease is recognized to be occurring in the local community or communities;
- (3) evidence that the local community or communities have a history of high rates of tuberculosis when compared to rates of tuberculosis for the nation or this state; or
- (4) evidence that children from populations having a high risk of tuberculosis are enrolled in the district or the non-public school; in this paragraph, "populations having a high risk" include groups that historically have been medically underserved, homeless persons, foreign-born persons from countries with high rates of tuberculosis, and persons with immune deficiency conditions.

(c) If the result of a PPD skin test is positive, including a test result provided under (f)(1) of this section, the district or non-public school shall refer the child to a health care provider

and notify the division at its office in Anchorage.

(d) The district or non-public school shall record the result of a PPD skin test administered under this section in the permanent health record of the child.

(e) The district or school shall suspend a child under AS 14.30.045 (4) if

- (1) the child fails to submit to a PPD skin test required under this section; or
- (2) the child or a person acting on behalf of the child fails to provide the district or non-public school, within 30 days after referral under (c) of this section, a written and signed statement of a health care provider stating that the child is not infectious from tuberculosis to others.

(f) Notwithstanding (a) - (e) of this section, a PPD skin test is not required under this section if the child or a person acting on behalf of the child provides the district or non-public school with

- (1) documentation showing
 - (A) negative results of PPD skin test administered within the preceding six months; or
 - (B) positive results at any time on the PPD skin test; or
- (2) the affidavit of a physician lawfully entitled to practice medicine or osteopathy in this state stating the opinion that the PPD skin test to be administered would be injurious to the health and welfare of the child or members of the family or household.

(g) A student whose PPD skin test obtained under (a) or (b) of this section has a positive result shall have a health evaluation, including a chest x-ray, by a health care provider. The

health care provider shall report the case to the section of epidemiology in the division.

7 AAC 27.215.

TUBERCULOSIS SCREENING OF SCHOOL EMPLOYEES.

(a) Each employee of each public school district, and of each non-public school, offering pre-elementary education through 12th grade education, or any combination of these grades, shall be evaluated annually, except as provided otherwise in this subsection, to detect active cases of pulmonary tuberculosis, as follows:

(1) an employee who has never had a positive tuberculin skin test result shall obtain a tuberculin skin test;

(2) an employee who has previously had a positive tuberculin skin test result, or an employee whose tuberculin skin test obtained under (1) of this subsection has a positive result,

(A) shall have a health evaluation by a health care provider to identify symptoms suggesting that tuberculosis disease is present; the health evaluation must also include evaluation for the presence of any of the following risk factors: evidence of inadequately treated past tuberculosis disease, history of close exposure to a case of communicable pulmonary tuberculosis within the previous two years, history of a negative tuberculin test within the previous two years, diabetes mellitus (severe or poorly controlled), diseases associated with severe immunologic deficiencies, immunosuppressive therapy, silicosis, gastrectomy, excessive alcohol intake, or human immunodeficiency virus infection; if symptoms suggesting tuberculosis disease are present, or if any of the risk

factors is present, a chest x-ray shall be obtained as part of the health evaluation and the health care provider shall report the case to the section of epidemiology, division of public health; and

(B) if the employee has previously received appropriate antituberculosis chemotherapy and has no symptoms suggesting that tuberculosis is present, the employee need not have further annual tuberculosis evaluation under this subsection.

7 AAC 27.890.

CONFIDENTIALITY OF ALL REQUIRED REPORTS AND MEDICAL RECORDS.

(Note: In this section, "this chapter" means 7 AAC Chapter 27.)

(a) A report to the division required under this chapter is a confidential public health record and is not open to public inspection.

(b) A medical record provided to the division by a physician, surgeon, hospital, laboratory, out-patient clinic, nursing home, or other facility, individual, or agency providing services to patients that identify cases or establishes characteristics of the status of an identifiable patient with a condition reportable under this chapter is confidential and may not be disclosed to the public.

7 AAC 55.190.

CAREPROVIDER QUALIFICATIONS.

repealed 3/1/98

7 AAC 55.220.

ADMISSION PROCEDURES.

repealed 3/1/98

7 AAC 55.270.

HEALTH PROGRAM.

repealed 3/1/98

7 AAC 75.220.

GENERAL EMPLOYMENT REQUIREMENTS.

(a) Except as provided in (d) of this section, an individual may not be employed by an assisted living home as an administrator or care provider unless the individual provides

(1) to the home a sworn statement as to whether the individual has, before being hired by the home, been convicted of a

(A) felony;

(B) misdemeanor involving drugs or physical or sexual abuse; or

(C) misdemeanor involving alcohol;

(2) to the home, at the time requested by the home before hiring, the results of a name-check criminal background investigation that has been conducted by the Alaska Department of Public Safety no more than 30 days before the individual is hired; and

(3) to the home, at the time requested by the home before hiring, the names, addresses, and telephone numbers of

(A) three persons, unrelated to the individual, who will provide character references for the individual; and

(B) two employment references; and

(4) evidence, at the time requested by the home before hiring, that the individual is free from active pulmonary tuberculosis before contact with residents and annually after hiring.

(b) Within 90 days after an individual is hired, the individual shall provide to the home the results of a fingerprint criminal background investigation conducted by the Alaska Department of Public Safety.

(c) An assisted living home may not retain an administrator or care provider whose fingerprint criminal background history

reveals material information not disclosed on the sworn statement required by (a)(1) of this section.

(d) An individual who, before employment by a home, has been convicted of a crime described in (a)(1) of this section may serve as an employee of an assisted living home if the individual

(1) truthfully reveals that information at the time of employment; and

(2) provides evidence satisfactory to the home and the licensing agency that the individual does not pose a risk to residents and will not adversely affect the safety or effective operation of the home.

(e) An individual who, after employment by an assisted living home, is convicted of a crime described in (a)(1) of this section may, at the discretion of the owner or governing body of the home and with the approval of the licensing agency, continue as an employee if the crime did not and does not pose a risk to residents or adversely affect the safety and effective operation of the home.

12 AAC 14.500.

PRENATAL CARE.

(a) The board recommends that a certified direct-entry midwife make prenatal visits to a client every four weeks until the 28th week of gestation, every two weeks from the 29th through the 35th week of gestation, and weekly from the 36th week of gestation until birth.

(b) At the initial prenatal visit, the certified direct-entry midwife shall recommend that the client undergo a physical examination as required in AS 08.65.140 to screen for health problems that could complicate the pregnancy or delivery and that includes a review of the laboratory studies required in (c) of this section. The certified direct-entry midwife shall obtain a signed written consent from the client

reflecting the client's informed choice regarding the recommended physical examination and retain the consent in the client's record.

(c) At the initial prenatal visit, the certified direct-entry midwife shall

(1) order the following laboratory tests:

- (A) a serological test for syphilis, either rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL);
- (B) blood group;
- (C) Rh factor and screen;
- (D) rubella titer;
- (E) complete blood count;
- (F) gonorrhea screen; and
- (G) urinalysis;

(2) recommend the following laboratory tests:

- (A) test for tuberculosis; and
- (B) test for hepatitis and human immune deficiency virus (HIV).

(d) At 15 - 20 weeks of gestation, the certified direct-entry midwife shall discuss with the client the availability of maternal serum alpha-fetoprotein screening.

(e) At 24 - 28 weeks of gestation, the certified direct-entry midwife shall recommend a 50 gm glucose tolerance test for gestational diabetes.

(f) At 28 and 36 weeks of gestation, the certified direct-entry midwife shall order a hemoglobin or hematocrit test, and, for a woman with Rh negative type blood, an antibody screen.

(g) At each prenatal visit, the certified direct-entry midwife shall order the analysis of a clean catch urine sample for glucose and protein.

(h) The certified direct-entry midwife shall comply with AS 08.65.140(b) in obtaining a signed informed consent for home delivery.

(i) During the third trimester, the certified direct-entry midwife shall consult with the client concerning selection of a pediatrician, family physician, or other health care provider who will assume responsibility for the infant. The certified direct-entry midwife shall record the client's choice in the client's record. If the client cannot or will not select a provider for the infant, the certified direct-entry midwife shall document this information in the client's record.

(j) The certified direct-entry midwife shall consult with a physician if, during the prenatal period, the client

- (1) develops 2 + or greater pitting edema on the face and hands;
- (2) develops consistent glucosuria or proteinuria of 1 + or greater;
- (3) has marked or severe polyhydramnios or oligohydramnios;
- (4) prior to 37 weeks gestation, has six or greater contractions per hour not resolved with hydration or rest, or has effacement or dilation of the cervix;
- (5) has severe protruding varicose veins of the extremities or vulva;
- (6) develops blood pressure of 140/90 or an increase of 30 mm Hg systolic or 15 mm Hg diastolic over the usual blood pressure;
- (7) develops severe, persistent headaches, epigastric pain, or visual disturbances;
- (8) has symptoms of urinary tract infection such as a rise in temperature, kidney or flank pain, urinary frequency, or dysuria;
- (9) has rupture of membranes before 37 weeks gestation;

- (10) has marked decrease or cessation of fetal movement;
- (11) has fetal heart tones of less than 100 or more than 170 per minute;
- (12) has inappropriate gestational size;
- (13) has fever of 100.4 F. or 38 C. for 24 hours or more;
- (14) has severe or ongoing medical complications;
- (15) has demonstrated anemia by blood test (hematocrit 27 percent or hemoglobin 9 grams);
- (16) is found to have a positive antibody screen;
- (17) has vaginal bleeding other than show before the onset of labor;
- (18) fails a three-hour oral glucose tolerance test; or
- (19) has a positive purified protein derivative (PPD) test, hepatitis screen, or human immune deficiency virus (HIV) test.

(k) If, following the consultation set out in (j) of this section, the physician recommends referral for immediate medical care the certified direct-entry midwife shall refer the client for immediate medical care. A referral for immediate medical care does not preclude the possibility of a home delivery if, following the referral, the client does not have any of the conditions set out in AS 08.65.140 (d).

(l) During the third trimester, the certified direct-entry midwife shall ensure that the client is adequately prepared for a home birth by discussing issues such as sanitation, facilities, adequate heat, availability of telephone and transportation, plans for emergency evacuation to a hospital, and the skills and equipment that the midwife will bring to the birth.

(m) A certified direct-entry midwife shall make a home visit three to five weeks before the estimated date of confinement to assess the physical environment, to determine whether the client has the necessary supplies, to prepare the family for the birth, and to instruct the family in correction of problems or deficiencies.

13 AAC 08.025.

MEDICAL STANDARDS.

(a) A school bus driver permit may not be issued to a person who does not meet the following minimum standards as certified by a medical doctor, a physician's assistant licensed by the State Medical Board, or an advanced nurse practitioner licensed by the Board of Nursing, on the form required in 13 AAC 08.015(1):

- (1) the person must be free of communicable disease at the time of examination;
- (2) the person must have a chest X-ray or "skin test" that shows the person to be free of tuberculosis;
- (3) the person's visual acuity may not be less than 20/30 in one eye and 20/200 in the other eye, either with or without corrective lenses;
- (4) the person may not have monocular vision;
- (5) the person may not have a history of fainting spells, dizziness, convulsions, epilepsy, or cardiac ailment during the 12 consecutive months immediately preceding the examination;
- (6) the person must have normal use of both hands, arms, and feet;
- (7) the person may not have a physical disability that would prevent safe operation of a school bus under all driving conditions;

(8) the person may not presently be under treatment for excessive use of alcohol or drugs.

(b) Except as provided in (c) of this section, a renewal of a school bus driver permit may not be granted unless the requirements of (a) (1)-(8) of this section are met.

(c) When a person has a "skin test" that does not show the person to be free of tuberculosis, a chest X-ray is not required under (a)(2) of this section if within 18 months before the skin test the person had a chest X-ray that showed him to be free of tuberculosis. Nothing in this section, however, prevents the person conducting the examination from concluding that the X-ray is necessary for diagnostic purposes and requiring that an X-ray be taken.

(d) A report of an examination performed under this section by a physician's assistant or an advanced nurse practitioner must be signed by that person, and include the name of the collaborating physician.

22 AAC 05.121.

PRISONER RESPONSIBILITY FOR HEALTH CARE SERVICES.

(a) A prisoner will be provided medically necessary health care services regardless of the prisoner's ability to pay or arrange for payment or coverage for the services. Medically necessary health care services include medical, psychological, and psychiatric care that is necessary to enable a prisoner to participate in or benefit from rehabilitative services made available by the department.

(b) Except as provided in (c) and (d) of this section, a prisoner

(1) is financially responsible for a co-payment for health care services provided to the prisoner by the department through department employees or designated contractors; and

(2) shall arrange for the department to obtain payment or coverage from one or more of the responsible parties set out in AS 33.30.028 (a), if the prisoner receives health care services not provided through department employees or designated contractors.

(c) The department will not pursue payment by a prisoner for the following inspections, examinations, or testing required by state regulation or necessary to protect the health or safety of the general prisoner population or others:

(1) inspection upon initial admission provided under 22 AAC 05.005;

(2) a physical examination under 22 AAC 05.120 (b);

(3) testing for pregnancy, HIV, AIDS, tuberculosis, sexually transmitted diseases, or other communicable diseases.

(d) The department will not pursue the co-payment from a prisoner for the following health care services provided under circumstances listed, so long as the prisoner arranges for the department to obtain payment or coverage from one or more of the responsible parties set out in AS 33.30.028(a) to the extent that such payment or coverage is available:

(1) services for injuries or repair or replacement of medical equipment if the services resulted from work performed for the department or an assault or violation of facility rules or state law by another prisoner, but only if the services were not due to the prisoner's failure to follow medical instructions or to protect the equipment against loss or damage;

(2) services initiated by health care providers who are department employees or designated contractors;

(3) services for communicable diseases or pregnancy;

(4) treatment for a chronic disease or medical or mental condition, if after consulting with appropriate health care providers, the department determines that the potential for harm to the prisoner is substantial if treatment is delayed.

(e) Notwithstanding (a) - (d) and (g) of this section, a prisoner may be charged for the full cost of health care services provided by health care providers other than department employees or designated contractors, resulting from a self-inflicted injury, or an injury to the prisoner or to another prisoner resulting from an assault or other violation of facility rules or state law by the prisoner.

(f) A prisoner who is provided health care services by a departmental employee or designated contractor is financially responsible for the following co-payments:

SERVICE CO-PAYMENT

Health care services by a health care provider \$4 for each visit or service

Health care services provided under (d)(2) of this section for injuries incurred in sports activities, if the activity was recommended against by a health care provider \$4 for each visit or service

Initial prescriptions or changes or renewals in prescriptions ordered at the same time \$4

Use of medical equipment available in the facility, such as crutches or Neoprene braces \$4 per use

(g) Notwithstanding (b) of this section, the department will not pursue payment by the prisoner for the cost of the use of medical equipment not available in the correctional facility above the first \$20 charged for each use by the prisoner.

(h) The department will deduct the co-payments and cost of health care services as provided in this section for which a prisoner is responsible directly from the prisoner's prison fund account. However, such deductions are subject to outstanding obligations of the prisoner to pay that are given a higher priority under the law, such as child support orders, court-ordered restitution, civil judgments or administrative orders resulting from the prisoner's criminal conduct, court-ordered fines, and restitution ordered by the department. A prisoner residing in a community residential center has an additional priority deduction of payment for room and board as determined by the department. The prisoner must be notified in writing of the deduction made under this subsection.

(i) A prisoner may challenge the amount deducted under (h) of this section by submitting a written appeal to the health care officer in the facility within three working days of receiving notice of the deduction. The appeal must set out reasons why the amount deducted is incorrect. The health care officer shall issue a written decision. The prisoner may appeal the decision to the director of institutions of the department. The appeal must be made within seven working days of the prisoner's receiving notice of the health care officer's decision. The decision of the director of institutions is the final departmental decision, and must be made in writing. If the director of institutions grants the appeal, the prisoner's prison fund account will be adjusted consistent with that decision.

(j) In this section,

(1) "AIDS" means acquired immunodeficiency syndrome;

(2) "community jail" is a jail owned or operated by a municipality of the state that confines prisoners held under the authority

of state law under a contract with the department under AS 33.30.031 ;

(3) "co-payment" is that portion of the cost of health care services provided by a department employee or designated contractor for which the department will pursue payment directly from the prisoner;

(4) "correctional facility" has the meaning given in AS 33.30.901;

(5) "designated contractor" means a health care provider who

(A) is not employed by the department; but

(B) does have a collaborating or supervisory relationship with a health care provider who is an employee of the department, or has a written contract that provides for payment by the department other than on a per patient visit basis;

(6) "health care officer" is the chief departmental health care provider in a correctional facility;

(7) "health care provider" includes a physician, psychiatrist, psychologist, emergency medical technician, physician assistant, registered or practical nurse, advanced nurse practitioner, dentist, dental hygienist, optometrist, pharmacist, mental health clinician, clinical social worker, psychological associate, dispensing optician, physical therapist, and occupational therapist;

(8) "health care services" means medical, psychological, and psychiatric care, including medical equipment, provided under AS 33 by a health care provider; "health care services" do not include sex offender or substance abuse treatment provided by the department;

(9) "HIV" means human immunodeficiency virus;

(10) "medical care" includes any evaluation, treatment, medication, medical equipment, or consultation given by a health care provider, related to any physical, mental, dental, auditory, or optometric condition; "medical care" does not include psychological and psychiatric care given by a health care provider;

(11) "official detention" has the meaning given in AS 11.81.900 (b);

(12) "prisoner" means a person in the custody of the department in the state in official detention; "prisoner" includes a person who has been released by the department on an authorized furlough or confined in a restitution center or other correctional facility, but not including a community jail;

(13) "psychological and psychiatric care" includes any evaluation, treatment, medication, or consultation given by an appropriate health care provider for a mental or social adjustment condition that is not "medical care" under this section.

Appendix 2. Forms and Instructions

Screening Form for Persons with a Positive Tuberculin Skin Test

Tuberculosis Questionnaire/Request for Chest X-Ray Interpretation

Drug Order and Refill Request (Form 10)

Record of Examination of Close Contacts of Active Cases or Associates of Recent Converter
(Form 43)

Patient Surveillance Report

Clinical Summary/Update/Chest X-Ray Interpretation - (formerly Form 17)

Examination for Tuberculosis - (Form 06-1216)

School Tuberculin Testing Report - (Form 41)

Consent for Release of Medical Information

Hospital Discharge Plan for Patients with Tuberculosis

Clinic Code _____ Walkin/Appt

Tx Code 01 02 04 07 09 12 30 31

AT _____ TT _____

Medicaid# _____

Sec Prov

Prim Prov

State of Alaska
Department of Health and Social Services
Screening Form for Persons with a Positive Tuberculin Skin Test, Page 1

This checklist can be used by public health nurses to determine if a client found to have a positive skin test can be cleared for school or work. **This determination should only be made after a Mantoux (PPD) skin test has been done.** Since many persons with a positive skin test will be candidates for therapy for latent TB infection (LTBI), Page 2 of the form should be used to determine if the client, even though cleared for school or work, should still be referred to their health-care provider.

Part 1. Work clearance -

Do you have any of the following symptoms?	Yes	No
a. Cough that has lasted more than 2 weeks?	_____	_____
b. Night sweats?	_____	_____
c. Coughing up blood or blood tinged sputum?	_____	_____
d. Recent unexplained weight loss?	_____	_____

If one or more of the answers to the above questions is "yes," the client should be referred for further evaluation. Copies of completed Parts 1 and 2 of this form, or preferably, a completed "Tuberculosis Questionnaire/Request for Client X-ray Interpretation" should be provided to both the health-care provider who will be doing the additional evaluation and the Tuberculosis Control Program.

If the answers to all the above questions are "no," continue with Part 2 to see if an evaluation for therapy for LTBI is warranted. Regardless of the answers to Part 2, the client can be cleared for school or work.

A-AI-C	#	Purpose of Visit/Problem List Additions or Changes

HR#: _____
Name: _____
B Date: _____ Sex: _____ Race: _____
Residence: _____
Facility: _____
Date: _____

(detach here)

Printed name of client: _____
Date of birth: _____

This person has been screened for active tuberculosis and has been cleared for work at this time.

Signature of screener: _____
Date: _____

Title: _____
Address: _____



Revised 2/9/2001

Screening Form for Persons with a Positive Tuberculin Skin Test, Page 2

Many persons with a positive tuberculin skin test will benefit from treatment of LTBI. The following questions can help determine if a client should be referred for further evaluation. **An answer in any of the boxed areas indicates that the client should be referred to a physician, nurse practitioner, or physician assistant.** Generally, persons who have received a complete course of LTBI treatment in the past do not need rescreening. A more detailed explanation of the indications for recommending treatment of LTBI can be found in the chapter "Treatment of Latent Tuberculosis Infection" in the manual.

Part 2. Screening for therapy for LTBI -

- | | | |
|--------------------------|--------------------------|--|
| Yes | No | |
| <input type="checkbox"/> | <input type="checkbox"/> | 1. Have you ever been ill with tuberculosis? |
| <input type="checkbox"/> | <input type="checkbox"/> | a. If so, did you take medicine for it? (Please document below) |
| <input type="checkbox"/> | <input type="checkbox"/> | b. Did you finish treatment? |
| <input type="checkbox"/> | <input type="checkbox"/> | 2. Have you taken medicine in the past to prevent tuberculosis disease? (Please document below) |
| <input type="checkbox"/> | <input type="checkbox"/> | a. If so, did you finish treatment? |
| <input type="checkbox"/> | <input type="checkbox"/> | 3. Have you had a negative skin test at any time during the past 2 years? |
| <input type="checkbox"/> | <input type="checkbox"/> | 4. Have any members of your household or family or any of your close friends had tuberculosis during the past 2 years? |
| <input type="checkbox"/> | <input type="checkbox"/> | 5. Do you have any of the following diseases or illnesses: |
| <input type="checkbox"/> | <input type="checkbox"/> | a. HIV/AIDS or unknown HIV status with risk factors for HIV? |
| <input type="checkbox"/> | <input type="checkbox"/> | b. diabetes (severe or poorly controlled)? |
| <input type="checkbox"/> | <input type="checkbox"/> | c. silicosis? |
| <input type="checkbox"/> | <input type="checkbox"/> | d. any disease which affects the immune system such as cancer or leukemia? |
| <input type="checkbox"/> | <input type="checkbox"/> | e. any medical treatment using steroids, radiation or x-rays? |
| <input type="checkbox"/> | <input type="checkbox"/> | f. alcohol use to an extent that it has caused a problem in your family, health or job? |
| <input type="checkbox"/> | <input type="checkbox"/> | g. severe kidney disease? |
| <input type="checkbox"/> | <input type="checkbox"/> | h. use of intravenous drugs? |
| <input type="checkbox"/> | <input type="checkbox"/> | i. stomach surgery (gastrectomy) or weight loss due to undernutrition? |
| <input type="checkbox"/> | <input type="checkbox"/> | 6. Were you born in a foreign country? |
| <input type="checkbox"/> | <input type="checkbox"/> | 7. Is your age less than 18 years? |

Documentation of Treatment* (complete only if answers to 1a or 2 are "yes")

Name of drugs (s)	Did you take this drug?			When did you take this drug?	
	Yes	No	Unknown	start date	stop date
isoniazid	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
rifampin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
ethambutol	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
pyrazinamide	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>
other	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="text"/>

*Note a detailed explanation of acceptable treatment regimens can be found in the chapter "Treatment of Tuberculosis Disease" in the manual. Clients with inadequately treated tuberculosis should be discussed with Tuberculosis Control Program staff.

Name: _____

Date: _____

Revised 2/9/2001

**Instructions for Completing
“Drug Order and Refill Request”
(Form 10)**

This form is used by public health nurses to order anti-tuberculosis drugs for individuals or for stock. Blank forms are available from the Tuberculosis Control Program.

Identifying Information: Give the patient’s name, birthdate and address. (Note: If ordering stock medications, write “STOCK” for the patient’s name.)

Drug Prescription: Provide the name of the physician who has prescribed the medicines and the period of time for which they were prescribed. If the time period for which drugs were prescribed differs from the period during which they will actually be administered, then indicate the date drugs were (or will be) started and the date they should be finished.

Time Period for Which Drugs are Needed: A 3-month supply of drugs should normally be ordered. Supplies can be ordered for a longer period of time under special circumstances.

Drugs and Dosage Size(s): Circle the name of the drug(s) being ordered and the size of the tablet or capsule.

Directions: Write directions you wish to appear on the bottle - for example, “one tablet daily” or “two capsules 2 hours before or after eating.”

Mail To: Indicate provider to whom medicines are to be mailed (note: medicines are not mailed directly to patients). Please allow 2 weeks for shipment of drugs for therapy for LTBI. In certain circumstances, drugs for TB cases may be expedited via air express. Please call the Tuberculosis Control Program to discuss such requests.

Person Requesting Drug(s): Write name, city, and phone number of person who has requested the medicine.

Distribution: Send original and one copy to the Tuberculosis Control Program. Keep a copy for your record until you know the drugs have been received.

**Instructions for Completing
“Record of Examination of Close Contacts of Active Case
or Associates of Recent Converter”**

This form is available from the Tuberculosis Control Program. It is used by public health nurses to assist in the examination of contacts of active cases of tuberculosis and identification of the source of infection among the associates of tuberculin converters or children less than 6 years of age as well as to provide statistical information. An initial copy of the form should be submitted as soon as the first round of PPDs are completed. A final copy should be submitted on completion of contact follow-up.

NAME OF PATIENT, ADDRESS, ETC:

Self-explanatory. Indicate results of sputum AFB smear and sputum mycobacterial culture, if known.

CONTACTS OR ASSOCIATES

Name, Birthdate, Sex, Household (in-Out), Relation to Above: List and complete identifying information about close contacts to case or associates of converters or reactor. Indicate whether the contact or associate resides inside the patient’s household (“IN”) or elsewhere (“OUT”).

Date of 1st Exam: Give date and type (x-ray, sputum) of first examination. If no examination, give reason. If contact not living in your area, indicate to whom referral was made.

Symptom Screening: If screening a previously known positive individual, enter date of symptom screen.

Date Rx for LTBI Started: Enter date if patient is currently taking treatment for LTBI.

Date of Previous Treatment for LTBI: If known, enter date of previous treatment.

Previous Rx for Active TB: Record date and place of previous treatment, if known.

Date and Results of Second PPD: Three months after contact with active case of pulmonary tuberculosis with positive sputum was broken, report (on a copy you have kept) the results of the second examination of close contacts who were tuberculin negative when first examined. For individuals who convert their PPD on the 2nd test, please record the date of their CXR in the x-ray field.

DISTRIBUTION: After the initial contact or associate investigation, send the **white** and **green** copies to the regional nurse manager or health care supervisor. The **white** copy should then be forwarded to the Tuberculosis Control Program. After completion of the second round of PPD skin testing, send the **yellow** copy to the Tuberculosis Control Program. Keep the **pink** copy for the patient’s medical chart or health center files.

Case Number: 401000404
 Date: 02/04/2014

Case Name: _____
 Address: _____
 City: _____

Sex: _____
 Date of Birth: _____

Diagnosis: _____
 Date of Diagnosis: _____

Local Health Unit: _____

Case Status: _____

Case Manager: _____

Case Start Date: _____

Case End Date: _____

Case Duration: _____

Case Priority: _____

Case Status: _____

Case Notes: _____

Case Comments: _____

Case History: _____

Case Summary: _____

Case Conclusion: _____

Visit Location: _____

Public Health Nurse: _____

Date: _____

Instructions for Completing "Patient Surveillance Report"

These reports are generated by the Tuberculosis Control Program. They are sent to each public health nurse who has patients being treated for latent TB infection (LTBI). Because of the new short treatment regimens, reports will be generated approximately 1-3 months after patients should have completed therapy.

SECTION 1 - Date treatment of LTBI completed:

If a patient has completed the prescribed course of treatment for LTBI, provide the date treatment was completed. Note that this section applies only to patients who have completed a full course of treatment.

Example #1

An adult patient starts isoniazid 1/01/00 and finishes taking 9 months of medication on 12/01/00. He has taken 9 months of medication in 11 months time. Enter: Date LTBI treatment completed: 12/01/00.

Example #2

A child starts isoniazid 1/01/00 and stops on 10/01/00. He missed 1 monthly refill and took a total of 8 months of medication in 9 months. He refuses to take another month of isoniazid. Selection: Since this child did not complete the 9 month treatment regimen for LTBI, a response from Section 3 must be chosen.

SECTION 2 - Regimen for LTBI

Mark the drug regimen the patient is taking. Note: The only recommended regimen for children is a 9 month course of isoniazid.

SECTION 3 - Reason therapy for LTBI was discontinued before completion

Under this section are listed reasons treatment of LTBI was not completed.

Note the distinction between 3(a) and 3(b). 3(a) should be selected if treatment of LTBI was "discontinued by physician due to adverse reaction." 3(b) should be selected if treatment is "discontinued on medical advice for reason other than adverse reaction." For example, a 2-year-old household contact of a pulmonary tuberculosis patient is started on therapy for LTBI even if the first Mantoux skin test was 00 mm. If the skin test 3 months later was still 00 mm and isoniazid was discontinued by the child's physician, 3(b) would be the appropriate choice. If 3(d) is selected, please document attempted outreaches (i.e., letters, telephone calls). If 3(e) is selected, please provide a forwarding address.

Patient Surveillance Report

Name: _____ DOB: _____ Age: _____

Street: _____

State: _____ Zip code: _____

Date LTBI treatment started: ____/____/____

Please return form by: ____/____/____

PLEASE COMPLETE SECTION 1 (if patient finished prescribed course of treatment for LTBI) OR SECTION 3 (if patient did not complete treatment). IF 3(a), 3(b), OR 3(c) IS THE MOST APPROPRIATE RESPONSE, PLEASE ENTER THE DATE ON WHICH MEDICATION WAS STOPPED. Please indicate which regimen patient was taking in Section 2.

SECTION 1

Date LTBI treatment completed:

____/____/____

OR

SECTION 2

Regimen:

9 months INH _____

6 months INH _____

4 months RIF _____

2 months RIF/PZA _____

SECTION 3

Reason LTBI treatment was discontinued before completion:

a. ___ Discontinued by physician due to adverse reaction.

Date ____/____/____

b. ___ Discontinued on medical advice for reason other than adverse reaction.

Date ____/____/____

c. ___ Discontinued by patient against medical advice.

Date ____/____/____

d. ___ Patient lost to follow-up.

Attempted outreaches: letter(s) _____ phone call(s) _____

e. ___ Patient moved.

Forwarding address: _____

f. ___ Patient died.

g. ___ Patient developed tuberculosis disease.

Return to:
State of Alaska
Section of Epidemiology
Tuberculosis Control Program
P.O. Box 240249
Anchorage, AK 99524-0249

Examination for Tuberculosis - (Form 06-1216)

State of Alaska Public Health Laboratories

ANC
 Results.

TUBERCULOSIS

Date Recd _____ Lab No _____

Initial _____ Date Recd _____

DO NOT WRITE ABOVE THIS LINE

Patient's Name _____ Male Female

Last First Initial

Patient's Address _____ Race _____

Date of Birth _____ Patient ID No _____

Specimen Source _____ Date Collected: _____ Time Collected _____

Submitted By _____ M.D. _____ City _____

Physician Name

Address _____ Zip _____

© 1978 Alaska Dept. of Health

Instructions

This form should accompany all specimens submitted to the State Public Health Laboratories for examination for tuberculosis (mycobacterial cultures and AFB smears). The form and postage paid mailers are available from the State Public Health Laboratory - Anchorage (4500 Boniface Parkway; Anchorage, AK 99507; telephone 907-334-2100). AFB smears are not routinely done on CSF, urine, blood, blood products, or stool.

- A. The physician, public health nurse, community health aide or their designee (not the patient) should complete the laboratory form. All data requested should be complete and legible.
1. Enter the name and address of the physician, public health nurse, or health aide collecting the specimen in the lower left-hand corner. Results will be distributed to the person designated on the "M.D." line. Without a submitter, results cannot be returned.
 2. The date the specimen was collected must be entered on the appropriate line.
 3. Name and date of birth should be identical for all specimens collected from the same person.
- B. Wrap the form around the metal inner container, NOT the plastic specimen container.

Results will be sent by mail to the Tuberculosis Control Program and to the submitter.

HOW TO COLLECT AND SEND SPECIMENS: SEE PAGES 40, 42-43.

**Instructions for Completing
"School Tuberculin Testing Report"
(Form 41)**

This form is used to report results of PPD tuberculin testing for school children. It is available from the Tuberculosis Control Program. It consists of three parts:

Part 1. Screening Summary

Fill in the number of students (continuing and new) in each grade (required grades are starred). Fill in the number of students for each of the four categories in compliance (negative PPD, newly positive PPD, previously positive PPD, or medical exemption).

NOTE: A copy of each medical exemption must be submitted with the screening summary.

Part II. Students with Newly-Positive PPD Skin Test Results

Fill in the name and requested information for each student with a newly-positive PPD skin test result. Provide the date and record the PPD reading in millimeters (mm).

NOTE: All students with newly-positive PPD skin test results should be referred to a medical provider or a public health nurse for further evaluation, including determination of need for treatment of latent TB infection.

Part III. Students Not Skin Tested by December 15

List only those students who did not receive a PPD skin test prior to December 15. Submit the top (white) copy to the Tuberculosis Control Program with the top (white) copies of Parts I and II by December 15.

If the student received a PPD skin test after December 15, indicate the result in the appropriate column and submit a copy to the Tuberculosis Control Program.

Distribution:

The top (white) sheet of Parts I, II, and III should be submitted to the Tuberculosis Control Program no later than December 15 of each year.

Alaska Department of Health and Social Services

Division of Public Health

Tuberculosis Control Program

Submit Report to:

State of Alaska
 TB Control Program
 P.O. Box 240249
 Anchorage, Alaska 99524-0249
DEADLINE: December 15th

School Name: _____
 Address: _____
 City: _____ Zip: _____
 Telephone Number: _____
 Principal's/Director's Name: _____
 Reported by: _____ Date: _____

Please check the appropriate box:

Public School
 Private School

School Tuberculin Testing Report

Part I. Screening Summary

Grade Level*	Number of Students in Grade		Groups in Compliance				For Official Use Only	
	Continuing Students	New Students**	Negative PPD Test***	Newly Positive PPD****	Previously Positive PPD****	Medical Exemption*****	Total # In Compliance	Total # Not In Compliance
Kindergarten*								
First								
Second								
Third								
Fourth								
Fifth								
Sixth								
Seventh*								
Eighth								
Ninth								
Tenth								
Eleventh								
Twelfth								

*The required grade levels will be marked with an asterisk for each school.
 **New Students* are those attending school in your district for the first time;
 (skin testing is required for these students irrespective of their grade level).
 ***Negative PPD at school or negative PPD within 6 months preceding enrollment.
 ****Include only students with PPD reading of 10 mm induration or greater as positive.
 *****Submit copy of affidavit of medical exemption with testing report.

Hospital Discharge Plan for Patients with Tuberculosis

In order to assure continuity of care, it is critical that all hospitalized patients with tuberculosis (TB) have a comprehensive discharge plan in place prior to leaving the hospital. The Alaska State TB Control Program and the public health nurse case manager (State, Municipality of Anchorage, or Native health corporation) must be notified of the case as early as possible during the admission in order to have sufficient time to develop the plan. A complete plan should be documented prior to patient discharge:

- Designated hospital staff member to notify State TB Control Program at least 3 days in advance of impending patient discharge. Discharge date: _____
- Consultation with State TB Control Program to assure that patient is cleared for commercial travel. Date of consultation: _____
- Patient has a confirmed appointment with their physician or health-care provider for follow-up. Health care provider: _____ Date of appointment: _____
Address: _____
Phone: _____
- Patient traveling to a rural area has at least a 1 week but no more than 2 week supply of TB medications.
- Patient has a residence to return to or housing has been arranged in coordination with the State TB Control Program.
- Patient understands that he or she will have a designated public health nurse case manager and will receive TB treatment using directly observed therapy (DOT).

PHN Case Manager: _____

Public Health Center: _____

Phone: _____

The Alaska State TB Control Program may be reached during business hours at 907-269-8000 and after hours at 1-800-478-0084. The Municipality of Anchorage TB Control Program may be reached during business hours at 907-343-4799.

Completed form should be distributed as follows:

- White copy to PHN case manager
- Green copy to doctor for follow-up appointment
- Yellow copy to Section of Epidemiology
- Pink copy to hospital patient record



Appendix 3. Federal Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Facilities, 1994

The following material has been extracted from guidelines published by the U.S. Centers for Disease Control and Prevention in October 1994 (CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13):1-132). Copies of the full document are available from the Tuberculosis Control Program.

Executive Summary

This document updates and replaces all previously published guidelines for the prevention of *Mycobacterium tuberculosis* transmission in health-care facilities. The purpose of this revision is to emphasize the importance of a) the hierarchy of control measures, including administrative and engineering controls and personal respiratory protection; b) the use of risk assessments for developing a written tuberculosis (TB) control plan; c) early identification and management of persons who have TB; d) TB screening programs for health-care workers (HCWs); e) HCW training and education; and f) the evaluation of TB infection-control programs.

Transmission of *M. tuberculosis* is a recognized risk to patients and HCWs in health-care facilities. Transmission is most likely to occur from patients who have unrecognized pulmonary or laryngeal TB, are not on effective anti-TB therapy, and have not been placed in TB isolation. Several recent TB outbreaks in health-care facilities, including outbreaks of multidrug-resistant TB, have heightened concern about nosocomial transmission. Patients who have multidrug-resistant TB can remain infectious for prolonged periods, which increases the risk for nosocomial and/or occupational transmission of *M. tuberculosis*. Increases in the incidence of TB have

been observed in some geographic areas; these increases are related partially to the high risk for TB among immunosuppressed persons, particularly those infected with human immunodeficiency virus (HIV). Transmission of *M. tuberculosis* to HIV-infected persons is of particular concern because these persons are at high risk for developing active TB if they become infected with the bacteria. Thus, health-care facilities should be particularly alert to the need for preventing transmission of *M. tuberculosis* in settings in which HIV-infected person work or receive care.

Supervisory responsibility for the TB infection-control program should be assigned to a designated person or group of persons who should be given the authority to implement and enforce TB infection-control policies. An effective TB infection-control program requires early identification, isolation, and treatment of person who have active TB. The primary emphasis of TB infection-control plans in health-care facilities should be achieving these three goals by the application of a hierarchy of control measures, including a) the use of administrative measures to reduce the risk for exposure to persons who have infectious TB, b) the use of engineering controls to prevent the spread and reduce the concentration of infectious droplet nuclei, and c) the use of personal respiratory protective equipment in areas where there is still a risk for exposure to *M. tuberculosis* (e.g., TB isolation rooms). Implementation of a TB infection-control program requires risk assessment and development of a TB infection-control plan; early identification, treatment, and isolation of infectious TB patients; effective engineering controls; an appropriate respiratory protection program; HCW TB training, education, counseling, and screening; and evaluation of the program's effectiveness.

Although completely eliminating the risk of transmission of *M. tuberculosis* in all health-care facilities may not be possible at the present time, adherence to these guidelines should reduce the risk to persons in these settings. Recently, nosocomial TB outbreaks have demonstrated the substantial morbidity and mortality among patients and HCWs that have been associated with incomplete implementation of CDC's *Guidelines for Preventing the Transmission of Tuberculosis in Health-Care Facilities, with Special Focus on HIV-Related Issues* published in 1990.* Follow-

up investigations at some of these hospitals have documented that complete implementation of measures similar or identical to those in the 1990 TB Guidelines significantly reduced or eliminated nosocomial transmission of *M. tuberculosis* to patients and/or HCWs.

*CDC. Guidelines for Preventing the Transmission of Tuberculosis in Health-Care Facilities, with Special Focus on HIV-Related Issues. MMWR 1990;39(No. RR-17).

TABLE 2. Elements of a tuberculosis (TB) infection-control program

Element	Risk Categories				
	Minimal	Very Low	Low	Intermeditate	High
Assigning responsibility					
Designated TB control officer or committee	R	R	R	R	R
Conducting a risk assessment					
Baseline risk assessment	R	R	R	R	R
Community TB profile: incidence, prevalence, and drug-susceptibility patterns	Y	Y	Y	Y	Y
Facility case surveillance (laboratory- and discharge-diagnosis-based)	C	C	C	C	C
Analysis of purified protein derivative (PPD) test results among health-care workers (HCWs)	N/A	V ¹	Y	every 6-12 mos	every 3 mos
Review of TB patient medical records	N/A	O ²	Y	every 6-12 mos	every 3 mos
Observation of infection-control practices	N/A	N/A	Y	every 6-12 mos	every 3 mos
Evaluation of engineering control maintenance	O ³	O ³	Y	every 6-12 mos	every 3 mos
Developing a TB infection control plan					
Written TB infection control plan	R	R	R	R	R
Periodically reassessing risk					
Reassessment of risk	Y	Y	Y	every 6-12 mos	every 3 mos
Identifying, evaluating, and initiating treatment for patients who may have active TB					
Protocol (clinical prediction rules) ⁴ for identifying patients who may have active TB	R	R	R	R	R
Protocol for diagnostic evaluation of patients who may have active TB ⁵	N/A	R	R	R	R
Protocol for reporting laboratory results to clinicians, infection-control practitioners, collaborating referral facilities, and appropriate health department(s)	N/A	R	R	R	R
Protocol for initiating treatment of patients who may have active TB ⁵	N/A	R	R	R	R

(continued on next page)

R=recommended; Y=yearly; C=continual; N/A=not applicable; O=optional; V=variable

TABLE 2 (continued). Elements of a tuberculosis (TB) infection-control program

Element	Risk Categories				
	Minimal	Very Low	Low	Intermeditate	High
Managing patients who may have TB in ambulatory-care settings and emergency departments					
Triage system for identifying patients who have active TB in emergency departments and ambulatory-care settings	R	R	R	R	R
Protocol for managing patients who may have active TB in emergency departments and ambulatory care settings	R	R	R	R	R
Protocol for referring patients who may have active TB to collaborating facility	R	R	N/A ⁶	N/A ⁶	N/A ⁶
Managing hospitalized patients who may have TB					
Appropriate number of TB isolation rooms ⁷	N/A	N/A	R	R	R
Protocol for initiating TB isolation	N/A	N/A	R	R	R
Protocol for TB isolation practices	N/A	N/A	R	R	R
Protocol for discontinuing TB isolation	N/A	N/A	R	R	R
Protocol for discharge planning	N/A	N/A	R	R	R
Engineering controls					
Protocol(s) for maintenance of engineering controls	O ³	O ³	R	R	R
Respiratory protection					
Respiratory protection program	N/A	V ¹	R	R	R
Cough-inducing and aerosol-generating procedures					
Protocol(s) for performing cough-inducing or aerosol-generating procedures	O	O ⁸	R	R	R
Engineering controls for performing cough-inducing or aerosol-generating procedures	O ³	O ⁸	R	R	R
Educating and training HCWs					
Educating and training HCWs regarding TB	R	R	R	R	R
Counseling and screening HCWs					
Counseling HCWs regarding TB	R	R	R	R	R
Protocol for identifying and evaluating HCWs who have signs or symptoms of active TB	R	R	R	R	R
Baseline PPD testing of HCWs	O ⁹	R	R	R	R
Routine periodic PPD screening of HCWs for latent TB infection	N/A	V ¹	Y	every 6-12 mos	every 3 mos
Protocol for evaluating and managing HCWs who have positive PPD tests	R	R	R	R	R
Protocol for managing HCWs who have active TB	R	R	R	R	R

(continued on next page)

R=recommended; Y=yearly; C=continual; N/A=not applicable; O=optional; V=variable

TABLE 2 (continued). Elements of a tuberculosis (TB) infection-control program

Element	Risk Categories				
	Minimal	Very Low	Low	Intermeditate	High
Conducting a problem evaluation					
Protocol for investigating PPD conversions and active TB in HCWs	R	R	R	R	R
Protocol for investigating possible patient-to-patient transmission of <i>Mycobacterium tuberculosis</i>	R	R	R	R	R
Protocol for investigating possible contacts of TB patients who were not diagnosed initially as having TB and were not placed in isolation	R	R	R	R	R
Coordination with the public health department					
Effective system for reporting patients who have suspected or confirmed TB to appropriate health department(s)	R	R	R	R	R

R=recommended; Y=yearly; C=continual; N/A=not applicable; O=optional; V=variable

Notes:

- 1) Because very low-risk facilities do not admit patients who may have active TB to inpatient areas, most HCWs in such facilities do not need routine follow-up PPD screening after baseline PPD testing is done. However, those who are involved in the initial assessment and diagnostic evaluation of patients in the ambulatory-care, emergency, and admitting departments of such facilities or in the outpatient management of patients with active TB could be exposed potentially to a patient who has active TB. These HCWs may need to receive routine periodic PPD screening. Similarly, these HCWs may need to be included in a respiratory protection program.
- 2) Because very low-risk facilities do not admit patients suspected of having active TB, review of TB patient medical records is not applicable. However, follow-up of patients who were identified during triage as possibly having active TB and referred to another institution for further evaluation and management may be useful in evaluating the effectiveness of the triage system.
- 3) Some minimal or very low-risk facilities may elect to use engineering controls (e.g., booths for cough-inducing procedures, portable high-efficiency particulate [HEPA] filtration units, ultraviolet germicidal irradiation units) in triage/waiting areas. In such situations, appropriate protocols for maintaining this equipment should be in place, and this maintenance should be evaluated periodically.
- 4) The criteria used in clinical prediction rules will probably vary from facility to facility depending on the prevalence of TB in the population served by the facility and on the clinical, radiographic, and laboratory characteristics of TB patients examined in the facility.
- 5) The protocols should be consistent with CDC/American Thoracic Society recommendations.
- 6) Protocols for referring patients who require specialized treatment (e.g., patients with multidrug-resistant TB) may be appropriate.
- 7) Based on maximum daily number of patients requiring TB isolation for suspected or confirmed active TB. Isolation rooms should meet the performance criteria specified in these guidelines.
- 8) If such procedures are used in the triage protocol(s) for identifying patients who may have active TB.
- 9) Minimal-risk facilities do not need to maintain an ongoing PPD skin-testing program. However, baseline PPD testing of HCWs may be advisable so that if an unexpected exposure does occur, conversions can be distinguished from positive PPD test results caused by previous exposures.

Appendix 4. Antibiotic Dosage Charts

The following tables were calculated based on specific dosages in milligrams per kilogram. In most cases, the dose shown will need to be rounded to a higher or lower amount depending on available drug formulations and the patient's history, clinical status, laboratory test results, etc. The maximum daily dose or maximum twice weekly (or thrice weekly) dose must always be considered.

Isoniazid Dose Chart*

(See pages 30, 59, and 60 for dosage recommendations)

Lb	kg	5 mg/kg	10 mg/kg	15 mg/kg	20 mg/kg	40 mg/kg
10	4.5	23	45	68	91	181
15	6.8	34	68	102	136	272
20	9.1	45	91	136	181	363
25	11.3	57	113	170	227	454
30	13.6	68	136	204	272	544
35	15.9	79	159	238	318	635
40	18.1	91	181	272	363	726
45	20.4	102	204	306	408	816
50	22.7	113	227	340	454	900
55	24.9	125	249	374	499	900
60	27.2	136	272	408	544	900
65	29.5	147	295	442	590	900
70	31.8	159	300	476	635	900
75	34.0	170	300	510	680	900
80	36.3	181	300	544	726	900
85	38.6	193	300	578	771	900
90	40.8	204	300	612	816	900
95	43.1	215	300	646	862	900
100	45.4	227	300	680	900	900
105	47.6	238	300	714	900	900
110	49.9	249	300	748	900	900
115	52.2	261	300	782	900	900
120	54.4	272	300	816	900	900
125	56.7	283	300	850	900	900
130	59.0	295	300	885	900	900
135	61.2	300	300	900	900	900

*The maximum dose is 300 mg if treated daily or 900 mg if treated twice or thrice weekly.

Note: Available formulations for isoniazid include 100 mg tablets, 300 mg tablets, and 1 g vials. Use of isoniazid syrup is discouraged because of unpredictable absorption. Isoniazid 150 mg and rifampin 300 mg are available in combination as Rifamate. Isoniazid 50 mg, rifampin 120 mg, and pyrazinamide 300 mg are available in combination as Rifater.

Rifampin Dose Chart*

(See pages 30, 59, and 60 for dosage recommendations)

Lb	Kg	10 mg/kg	20 mg/kg
10	4.5	45	91
15	6.8	68	136
20	9.1	91	181
25	11.3	113	227
30	13.6	136	272
35	15.9	159	318
40	18.1	181	363
45	20.4	204	408
50	22.7	227	454
55	24.9	249	499
60	27.2	272	544
65	29.5	295	590
70	31.8	318	600
75	34.0	340	600
80	36.3	363	600
85	38.6	386	600
90	40.8	408	600
95	43.1	431	600
100	45.4	454	600
105	47.6	476	600
110	49.9	499	600
115	52.2	522	600
120	54.4	544	600
125	56.7	567	600
130	59.0	590	600
135	61.2	600	600

*The maximum dose is 600 mg for daily, twice weekly, or thrice weekly treatment.

Note: Available formulations of rifampin include 150 mg capsules, 300 mg capsules, and 10 mg/ml syrup. Rifampin 300 mg and isoniazid 150 mg are available in combination as Rifamate. Rifampin 120 mg, isoniazid 50 mg, and pyrazinamide 300 mg are available in combination as Rifater.

Ethambutol Dose Chart*

(See pages 59 and 60 for dosage recommendations)

Lb	Kg	15 mg/kg	25 mg/kg	30 mg/kg	50 mg/kg
10	4.5	68	113	136	227
15	6.8	102	170	204	340
20	9.1	136	227	272	454
25	11.3	170	283	340	567
30	13.6	204	340	408	680
35	15.9	238	397	476	794
40	18.1	272	454	544	907
45	20.4	306	510	612	1021
50	22.7	340	567	680	1134
55	24.9	374	624	748	1247
60	27.2	408	680	816	1361
65	29.5	442	737	885	1474
70	31.8	476	794	953	1588
75	34.0	510	850	1021	1701
80	36.3	544	907	1089	1814
85	38.6	578	964	1157	1928
90	40.8	612	1021	1225	2041
95	43.1	646	1077	1293	2155
100	45.4	680	1134	1361	2268
105	47.6	714	1191	1429	2381
110	49.9	748	1247	1497	2495
115	52.2	782	1304	1565	2608
120	54.4	816	1361	1633	2722
125	56.7	850	1417	1701	2835
130	59.0	885	1474	1769	2948
135	61.2	919	1531	1837	3062
140	63.5	953	1588	1905	3175
145	65.8	987	1644	1973	3289
150	68.0	1021	1701	2041	3402
155	70.3	1055	1758	2109	3515
160	72.6	1089	1814	2177	3629
165	74.8	1123	1871	2245	3742
170	77.1	1157	1928	2313	3856
175	79.4	1191	1984	2381	3969
180	81.6	1225	2041	2449	4082
185	83.9	1259	2098	2517	4196
190	86.2	1293	2155	2585	4309
195	88.5	1327	2211	2654	4423
200**	90.7	1361	2268	2722	4536

*The maximum dose for children (≤ 12 years of age) being treated on a daily regimen is 2500 mg. The ATS/CDC has not established other maximums.

**Doses must be calculated individually for patients weighing more than 200 lbs (90.7 kg).

Note: Available formulations of ethambutol include 100 mg and 400 mg tablets.

Pyrazinamide Dose Chart*

(See pages 30, 59, and 60 for dosage recommendations)

Lb	Kg	15 mg/kg	30 mg/kg	50 mg/kg	70 mg/kg
10	4.5	68	136	227	318
15	6.8	102	204	340	476
20	9.1	136	272	454	635
25	11.3	170	340	567	794
30	13.6	204	408	680	953
35	15.9	238	476	794	1111
40	18.1	272	544	907	1270
45	20.4	306	612	1021	1429
50	22.7	340	680	1134	1588
55	24.9	374	748	1247	1746
60	27.2	408	816	1361	1905
65	29.5	442	885	1474	2064
70	31.8	476	953	1588	2223
75	34.0	510	1021	1701	2381
80	36.3	544	1089	1814	2540
85	38.6	578	1157	1928	2699
90	40.8	612	1225	2041	2858
95	43.1	646	1293	2155	3016
100	45.4	680	1361	2268	3175
105	47.6	714	1429	2381	3334
110	49.9	748	1497	2495	3493
115	52.2	782	1565	2608	3651
120	54.4	816	1633	2722	3810
125	56.7	850	1701	2835	3969
130	59.0	885	1769	2948	4000
135	61.2	919	1837	3062	4000
140	63.5	953	1905	3175	4000
145	65.8	987	1973	3289	4000
150	68.0	1021	2000	3402	4000
155	70.3	1055	2000	3515	4000
160	72.6	1089	2000	3629	4000

*Maximum dose: 2000 mg if prescribed daily, 3000 mg if prescribed thrice weekly, and 4000 mg if prescribed twice weekly.

Note: The only available formulation of pyrazinamide is 500 mg tablets; alternatively, it is available in the combination product Rifater as rifampin 120 mg, isoniazid 50 mg, and pyrazinamide 300 mg.

Index

A

Acid-fast bacilli (AFB), 9, 17, 41, 45, 52
Acquired immunodeficiency syndrome,
 and anergy, 23, 25
 and tuberculosis disease, 50
 and tuberculosis infection, 27 - 37
Active tuberculosis, 17
Adverse reactions, 60
 see also specific antibiotics
AFB, *see Acid-fast bacilli*
AIDS, *see Acquired immunodeficiency syndrome*
Allergic reactions to drugs, *see specific antibiotics*
American Academy of Pediatrics, 22, 31, 69
American Thoracic Society, 8, 22, 29, 69
Anergy testing, 25
Antibiotic susceptibility testing, 41
Antibiotics
 adverse reactions, 60
 first-line drugs, 60
 second-line drugs, 60
 see also Capreomycin, Ciprofloxacin, Cycloserine,
 Ethionamide, Isoniazid, Kanamycin, Ofloxacin,
 Para-aminosalicylic acid (PAS), Pyrazinamide, and
 Rifampin
Associate investigations, 11, 55 - 57, 69, 73
Atypical mycobacteria, 15

B

BACTEC, 41, 43
BCG, 8, 23 - 24, 69, 78
Booster phenomenon, 24
Bronchoscopy, 39

C

Capreomycin, 60, 66
Case definition, 44 - 45
Chemoprophylaxis,
 See Treatment of latent tuberculosis infection
Chemotherapy, *see Treatment regimens*
Chest x-ray, 12 - 13, 32 - 33, 43, 52
 payment for, 12, 43
Children
 treatment of, 50
 treatment of latent tuberculosis infection, 31
 tuberculin skin testing, 20 - 23

Ciprofloxacin, 60, 67
Clinical manifestations,
 of extrapulmonary tuberculosis, 18
 of pulmonary tuberculosis, 39
Completion of therapy, 53
Compliance problems, 51 - 52
 see also Directly observed therapy
Contact investigations, 11, 55 - 58, 73
Control Strategy, 11
Cycloserine, 60, 65

D

Detention, order for, 52
Diagnosis of tuberculosis, 39, 43 - 44
Diagnostic tools, emerging, 43 - 44
Directly observed therapy (DOT), 9, 11, 13, 35 - 36,
 47, 50 - 51, 59, 74 - 75, 77
Discharge planning, 47, 115
Droplet nuclei, 15, 16
Drug interactions, *see specific antibiotics*
Drug resistance, 49, 52, 59
Drug susceptibility testing, 41

E

Enablers, in treatment program, 11, 74
Ethambutol, 48, 59 - 60, 63
Ethionamide, 60, 65
Evaluation, pretreatment, 33, 50
Extrapulmonary tuberculosis, 18, 39, 49, 52

F

Face masks, 16
False negative skin tests, 22 - 23
Forms, 97 - 115

G

Gastric aspiration, 40, 42

H

Health-care workers, 70
HEPA filtration, 15, 40

High-performance liquid chromatography (HPLC), 44
HIV, *see Human immunodeficiency virus*
Hospital discharge plan, 47, 115
Human immunodeficiency virus,
 and anergy, 25
 and latent tuberculosis infection, 27, 29, 30-31
 and tuberculosis disease, 50

I

Immigrants, 28, 70, 77
Indigent, 53
Infant
 treatment of, 27-28
 treatment of latent tuberculosis infection, 31
 tuberculin Skin Testing, 19, 23
Infectiousness, 17
INH, *see Isoniazid*
Isoniazid, 8-9, 27, 29-36, 47, 59-61
 see also Treatment of latent tuberculosis infection
Isoniazid preventive chemotherapy,
 see Treatment of latent tuberculosis infection

K

Kanamycin, 60, 68

L

Laboratory testing, 33, 41-43
Latent tuberculosis infection, 8-9, 16-17, 21, 24,
 27-37
Levofloxacin, 67
Live virus vaccination, 23, 25
Liver function testing, 33, 35
Long-term care,
 screening, 71

M

M. tuberculosis, *see Mycobacterium tuberculosis*
Mantoux skin test, 20-22, 69
 adverse reactions, 25
 booster phenomenon, 24
 contraindications, 25
 false negative, 22
Masks, 16
Measles vaccination, 23, 25
Miliary tuberculosis, 18
Monitoring treatment of tuberculosis, 51-52
Mono-Vacc test, 22
 see also Tuberculin skin test

Multidrug-resistant tuberculosis, 32, 49, 59
Multiple-puncture skin tests, 22
 see also Tuberculin skin test
Mycobacterium tuberculosis, 15
 antibiotic susceptibility, 41
 emerging diagnostic tools, 43-44
 sputum culture, 40

N

Nephrotoxicity, *see specific antibiotics*
Noncompliant patients, 45, 52
 see also Directly observed therapy
Nontuberculous mycobacteria, 15

O

Ofloxacin, 60, 67

P

Para-aminosalicylic acid, 60, 66
Pathogenesis of tuberculosis, 16
Peripheral neuropathy
 and isoniazid, 36
Polymerase chain reaction testing, 44
PPD, *see Tuberculin skin test*
Pregnancy, 32, 49
Preventive therapy, *see Treatment of latent tuberculosis infection*
Prophylaxis, *see Treatment of latent tuberculosis infection*
Public Health Investigations, 55-57, 69, 73
Public health nurse's role, 73-78
Pulmonary tuberculosis
 compliance problems, 52
 contact evaluation, 55-57
 diagnosis, 39-45
 follow-up, 36
 primary type, 16
 reactivation type, 16
 reinfection, 57
 symptoms, 16
 treatment regimens, 47, 59-60
 see also Directly observed therapy
Pyrazinamide, 34, 59-60, 63
Pyridoxine, 36, 49

Q

Quarantine, 45, 52

R

Reporting requirements, 10, 47
Resistance, drug, 49, 59
Restriction of patients, 45, 51
Rifampin, 59, 60, 62
Rifampicin, 31

S

Screening for latent tuberculosis infection, 69 - 71
 BCG, 8, 23, 69
 see also Tuberculin skin test
Skin test,
 converter, 21
 reactor, 21
 see also Tuberculin skin test
Sputum, 39 - 40
 monitoring, 51 - 52, 74 - 75
Streptomycin, 59 - 60, 64

T

Tine test, *see Multiple-puncture skin tests*
Transmission of tuberculosis, 15
 and restriction of activities, 51
Travel, 51
Treatment of latent tuberculosis infection
 and old, healed tuberculosis, 27, 33
 contraindications, 34 - 35
 directly observed therapy (DOT), 9, 35 - 36
 follow-up, 36
 HIV positive, 30 - 31
 pretreatment evaluation, 33
 treatment regimens, 34
 who to treat, 33
Treatment regimens
 and pregnancy, 32, 49
 extrapulmonary tuberculosis, 49
 pulmonary tuberculosis, 47, 59
 tuberculosis infection, 29
 see also Directly observed therapy
Tubercle bacilli. *see Mycobacterium tuberculosis*
Tuberculin skin test,
 adverse reactions, 25
 and BCG, 8, 24
 boosting, 24
 contraindications, 25
 converter (defined), 21
 "doubtful reaction", 22
 false negative, 22
 interpretation, 21
 live virus vaccines, 23, 25

Mantoux skin test, 20, 69
multiple-puncture skin tests, 22
PPD tuberculin, 19
reactor (defined), 21
reading, 21
two-step testing, 22, 24, 57
Tuberculosis Control Program, 11 - 14
Two-step skin testing, 22, 24, 57

U

Uncooperative patients, 45, 52
 see also Directly observed therapy

V

Ventilation, 15, 56

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coughing up blood

POSITIVE SKIN TEST

Night Sweats

MALaise

Weight Loss

CHILLS

FEVER

HEMOPTYSIS

Loss of
Appetite

Think

difficulty
breathing

chest pains

TB!

fatigue

EXPOSURE TO
TUBERCULOSIS

failure to thrive

Abnormal X-ray

Cough

Anorexia

Significant Skin Test

Shortness
of Breath